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GWAS of Parkinson's disease clinical biomarkers in 12 longitudinal patients' cohorts

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Abstract

Background: Several reports have identified different patterns of Parkinson’s disease progression in individuals carrying missense variants in *GBA* or *LRRK2* genes. The overall contribution of genetic factors to the severity and progression of Parkinson’s disease, however, has not been well studied.

Objectives: To test the association between genetic variants and the clinical features of Parkinson’s disease on a genome-wide scale.

Methods: We accumulated individual data from 12 longitudinal cohorts in a total of 4,093 patients with 22,307 observations over a median of 3.81 years. Genome-wide associations were evaluated for 25 cross-sectional and longitudinal phenotypes. Specific variants of interest, including 90 recently-identified disease risk variants, were also investigated post-hoc for candidate associations with these phenotypes.

Results: Two variants were genome-wide significant. Rs382940(T>A), within the intron of *SLC44A1*, was associated with reaching Hoehn and Yahr stage 3 or higher faster (HR 2.04 [1.58, 2.62], P-value = 3.46E-8). Rs61863020(G>A), an intergenic variant and eQTL for *ADRA2A*, was associated with a lower prevalence of insomnia at baseline (OR 0.63 [0.52, 0.75], P-value = 4.74E-8). In the targeted analysis, we found nine associations between known Parkinson’s risk variants and more severe motor/cognitive symptoms. Also, we replicated previous reports of *GBA* coding variants (rs2230288: p.E365K, rs75548401: p.T408M) being associated with greater motor and cognitive decline over time, and *APOE* E4 tagging variant (rs429358) being associated with greater cognitive deficits in patients.

Conclusions: We identified novel genetic factors associated with heterogeneity of Parkinson’s disease. The results can be used for validation or hypothesis tests regarding Parkinson’s disease.

Main text:

Introduction

Parkinson's disease (PD) is clinically defined by its motor features of rigidity, bradykinesia, gait disturbance, and tremor. Although these prominent features are important for diagnosis, patients with PD also suffer from many non-motor features such as constipation, urinary incontinence, orthostatic hypotension, REM sleep behavior disorder (RBD), apathy, hyposmia, and cognitive impairment.¹ Moreover, patients develop motor complications, including wearing off and dyskinesia, as side effects of medication. The onset, intensity and progression of these different PD clinical features vary among individuals, and the mechanisms underlying this heterogeneity are not well understood.

Recent genome-wide studies have identified 90 common variants associated with the risk of PD, with an overall heritability estimated to be between 22-27%.^{2,3} While previous studies have indicated the importance of genetic contributions to disease risk, the contribution of genetic factors to PD progression and heterogeneity has not been well studied. Investigating genetic factors associated with disease progression and heterogeneity in disease presentation is an important step in elucidating the underlying molecular mechanisms and identifying better patient stratification in clinical trials.⁴

Longitudinal patient cohorts are powerful resources that can be used to explore the impact of genetics on the trajectory of PD-related phenotypes; the inherent precision of repeated measurements over time provides more power to detect these associations. However, the available number of participants in each study is usually not enough to conduct a genome-wide association study (GWAS). In this study, we accumulated 22,307 follow-up visits from 4,093 patients across 12 cohorts (Table 1) and performed meta-analyses of longitudinal GWAS on the progression markers of Parkinson's disease. Using the results from this meta-analysis, we evaluated how known risk variants, including the 90 recently identified variants for PD,³ *GBA* protein coding mutations, and *APOE* tagging variants were associated with the progression of phenotypes. To maximize the utility of this work to other researchers, we have made all results from this study publicly searchable and available for download.

(<https://pdgenetics.shinyapps.io/pdprogmetagwasbrowser/>)

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Methods

Cohorts

Twelve longitudinal cohorts of PD patients recruited across North America, Europe and Australia were included in our study. The following observational studies were included: the Drug Interaction with Genes in Parkinson's Disease (DIGPD), the Harvard Biomarkers Study (HBS), the Oslo Parkinson's Disease study (partly including retrospective data), the Norwegian ParkWest study (PARKWEST), the Parkinson's Disease Biomarker Program (PDBP), the Parkinsonism Incidence and Cognitive and Non-motor heterogeneity In Cambridgeshire (PICNICS), the Parkinson's Progression Markers Initiative (PPMI), and the Profiling Parkinson's disease study (PROPARK). The four cohorts included were randomized clinical trials: the Deprenyl and Tocopherol Antioxidative Therapy of Parkinsonism (DATATOP), the NIH Exploratory Trials in Parkinson's Disease Large Simple Study 1 (NET-PD_LS1), the ParkFit study (PARKFIT), and the Parkinson Research Examination of CEP-1347 Trial study with its subsequent prospective study (PreCEPT/PostCEPT). More details of these cohorts are described in Appendix. Participants' information and genetic samples were obtained under appropriate written consent and with local institutional and ethical approvals.

Phenotyping

Each cohort had a different set of recorded biomarkers and phenotypes associated with Parkinson's disease. We selected the following continuous and binomial biomarkers based on their clinical importance and availability. For continuous outcomes, we collected the scores of Hoehn and Yahr staging scale (HY),⁵ total and sub-scores of the Unified Parkinson's Disease Rating Scale (UPDRS) or the Movement Disorder Society revised UPDRS version (MDS-UPDRS),⁶ Mini-Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA)⁷ and the modified Schwab and England Activities of Daily Living Scale (SEADL). With the exception of the subscores of UPDRS/MDS-UPDRS part 4, total scores and the subscores of UPDRS and MDS-UPDRS were normalized to the population-baseline mean and standard deviation and converted to Z values. The subscores of UPDRS/MDS-UPDRS part 4, measuring complication of treatment, were normalized to the mean and standard deviation of all observations because the score was 0 at the baseline for the de-novo PD

cohorts. We also determined whether subjects were recorded as presenting the following binomial outcomes during participant visits: constipation, cognitive impairment, depression, daytime sleepiness, Hoehn and Yahr stage of 3 or worse (HY3), hyposmia, insomnia, motor fluctuation, REM sleep behavior disorder (RBD), restless legs syndrome (RLS), and an SEADL of 70 or less (SEADL70). Because study-specific criteria for these binomial outcomes were not consistent amongst the studies, we tried to use the common criteria for these binomial outcomes if we had access to the raw data from the studies. The details of the definitions of binomial outcomes are provided in the Supplemental Table 1.

Genetics data

The genotyping was conducted with NeuroX, a targeted chip for neurodegenerative disease,⁸ for NET-PD_LS1, a part of DIGPD (DIGPD_neuroX), HBS, PDBP, and PRECEPT. The rest of DIGPD (DIGPD_chip) were genotyped using Illumina Multi-Ethnic Genotyping Array. Participants in DATATOP, OSLO, PARKFIT, PARKWEST, PICNICS, and PROPARK were genotyped using Illumina Infinium OmniExpress array. Whole genome sequencing data was used for PPMI, with the detailed methods for genome sequencing provided on the PPMI website (<https://www.ppmi-info.org/>).

Variant inclusion criteria consisted of call rate > 0.95 , MAF > 0.01 , and Hardy-Weinberg equilibrium test statistic $> 1E-4$. Participants were excluded due to the following criteria: high-missingness ($> 5\%$ for genotyped variants), sex discordance, extreme heterozygosity (F statistics > 0.15), Non-European ancestry confirmed by joint analysis with HapMap 3 data using principal component (Outside of mean ± 6 SD in PC1 or PC2 for European reference samples) (International HapMap 3 Consortium et al., 2010), and excessive relatedness (pairwise kinships > 0.125). We used PLINK version 1.9 for the above filtering.⁹

For all samples and variants passing quality control, imputation was conducted for chromosome 1 to 22 using Minimac3 using the Haplotype Reference Consortium panel (HRC r1.1) and Eagle v2.3 for phasing at the Michigan Imputation Server¹⁰, with the exception of the whole genome sequenced PPMI dataset. SNPs with an imputation quality of R^2 less than 0.3 and MAF $< 1\%$ were excluded. After quality control, the number of variants were approximately 2.6 - 2.9 million in NET-PD_LS1, DIGPD_neuroX, HBS, PDBP, and PRECEPT; 7.7 - 7.8 million in PICNICS, PROPARK, PARKWEST, DATATOP, PARKFIT,

DIGPD, and OSLO; and 8.6 million in PPMI. Note that the cohorts genotyped by NeuroX had relatively less genome coverage than others.

Cohort-level analyses

We conducted a separate GWAS for each cohort per phenotype of interest. In addition, DIGPD cohorts were analyzed separately according to the genotyping array used (DIGPD_neuroX cohort and DIGPD_chip cohort). Each outcome was analyzed by an additive model with covariates. For the binomial outcomes at baseline visit, when the outcomes were positive for more than 5% of participants and >20 counts, logistic regression analyses were conducted. Those without the binomial outcome at baseline were followed-up until either censored or the development of the outcome. If more than 20 events were observed during follow-ups, the outcome was analyzed using cox proportional hazard models with time-varying covariates. For the analysis of continuous traits, linear mixed models were used to evaluate the variants' association for the outcome. Age at diagnosis, year from diagnosis to the observation, and sex were adjusted for in all analyses. In addition, the following covariates were associated with the outcome of interest in a backwards stepwise manner: quadratic age, quadratic years from diagnosis, years of education, medication status (levodopa usage, dopamine agonist usage, using either dopamine agonist or levodopa), and a Hoehn and Yahr score of 2 or more at the first observation (except for the models regressing for Hoehn and Yahr score itself or UPDRS motor score). These covariates were selected per study using Akaike's Information Criteria (AIC) for logistic models and Cox survival models, and conditional AIC (cAIC) for linear mixed effect models. The cohort level analyses were conducted with R (version 3.5.0 <https://www.r-project.org/>) and rvttests.¹¹ R package 'cAIC4' was used to calculate cAIC.¹²

Meta-Analyses

The results from cohort-level analyses were combined using an inverse variance weighted fixed effect model. If the study-specific genomic inflation factor was more than 1.2, the study was excluded from the meta-analysis. Five of the 204 GWAS were excluded based on these criteria. For other cohorts, the overall alpha error was corrected using the genomic inflation factor before the meta-analysis. Meta-analyses were carried out with METAL.¹³ From the

meta-analysis results, we only evaluated variants with $MAF > 0.05$ due to statistical power constraints. We also excluded variants with minor allele frequency variability greater than 15% across cohorts. Further exclusions at the meta-analysis level include variants with Cochran's Q-test for heterogeneity < 0.05 and a total participant $N < 1000$. The null hypothesis was tested with a significance level of $5E-8$ on a two-sided test. For genome-wide signals, additional visualization and functional analyses were conducted using LocusZoom,¹⁴ FUMA (<http://fuma.ctglab.nl/snp2gene/>, version 1.3.3d).¹⁵ FUMA is a web-based annotation tool using MAGMA to conduct gene-based tests, a gene-set analysis and a tissue expression analysis. We applied a default setting. Also, we explored in eQTLGen database (<http://www.eqtlgen.org/>)¹⁶ and meta-analyzed expression data in the brain accessible from the study by Qi et al.¹⁷

Associations with the variants of interest, including the recently identified 90 risk variants for PD, known *LRRK2* and *GBA* variants, and *APOE*, were extracted from the meta-analysis results. We exploratory evaluated the associations of these variants and clinical features based on the significance level of 0.05, applying the Bonferroni adjustment of a maximum of 25 tests per variant (raw P-value < 0.002).

The summary of analytical processes is shown in figure 1.

Data availability

The summary statistics of the meta-analysis results, including the ones which were not evaluated in this manuscript, are publicly available for convenient browsing and downloading. (<https://pdgenetics.shinyapps.io/pdprogmetagwasbrowser/>)

Results

Novel GWAS associations with PD progression markers

The cohort characteristics are provided in Table 1. Overall, we analyzed 4,093 participants with 22,307 longitudinal data points over a median of 3.81 years. These cohorts varied in the years between enrollment and diagnosis, as well as follow-up durations. DATATOP,

ParkWest, PPMI, and PreCEPT/PostCEPT enrolled untreated PD patients while others enrolled both treated and untreated patients. Considering the difference in design and recruitment strategies in the cohorts (Appendix), it is important to adjust for baseline characteristics as well as the follow-up lengths per cohort-level. All cohort-specific models for analysis are listed in Supplemental Table 2.

In total, 204 GWAS were conducted and combined into 33 meta-analyses. Eight meta-analyses were not evaluated because of the small number of total participants in the analyses (N total <1000). Those excluded were baseline analyses for RBD, RLS and SEADL70; and longitudinal analyses for constipation, daytime sleepiness, hyposmia, RBD, and RLS. Therefore, we investigated 9 binomial traits at baseline, 7 binomial traits for survival, and 9 continuous traits over the follow-ups. The genomic inflation factor was the mean value of 0.993, SD of 0.023, and the range was [0.951, 1.031] across meta-analyses. The study specific genomic inflation factors were provided in Supplemental Table 3.

One association with the progression of PD was of genome-wide significance (P-value < 5.00E-08). The minor allele of rs382940 (chr9:108058562T>A), an intronic variant of *SLC44A1*, was associated with a higher hazard ratio (HR) of reaching Hoehn and Yahr stage 3.0 or greater (HR 2.04 [1.58, 2.62], P-value = 3.46E-8 (Estimates in a random effect model, 1.97 [1.38, 2.81], P-value = 1.96E-4)). When considering the baseline observations, the minor allele of rs61863020 (chr10:112956055G>A), an intergenic variant, was significantly associated with the lower baseline OR of having insomnia (OR 0.63 [0.52, 0.75], P-value = 4.74E-8 (The same estimates and P-value in a random effect model)). Locus plots and forest plots for these two associations are shown in Figure 2. Cochran's Q statistics, I-square and forest plots all showed no evidence of heterogeneity for these associations. (Figure 2)

To evaluate the potential molecular mechanism for the two genome-wide signals, we explored eQTL datasets in blood and brain,^{16,17} and functional annotation of the GWAS summary statistics using FUMA. Although it is in a regulatory region of *SLC44A1*, rs382940 itself was not reported to be an eQTL in blood or brain. Gene-based tests using the GWAS summary statistics for reaching HY3 showed that *SLC44A1* was significant gene-wise (P-value = 5.8E-07 < Bonferroni correction threshold = 2.7E-6, supplemental figure 1). Rs61863020 was a significant eQTL for *ADRA2A* (α -2A adrenergic receptor) (P-value = 7.2E-4, the Bonferroni corrected P-value = 6.5E-3, up-regulation for A allele) in the brain.

In the meta-analysis results from the other clinical outcomes, rs382940 was associated with higher scores in the UPDRS part 2 and part 3 (UPDRS2_scaled: 0.36 [0.15, 0.57], P-value = 8.21E-04; UPDRS3_scaled: 0.29 [0.14, 0.45], P-value = 2.18E-04). These findings are consistent with the primary association of rs382940 and reaching HY3, which is a significant motor milestone (bilateral signs on clinical examination and the emergence of postural instability). Except for the association with having insomnia at baseline, rs61863020 was not significantly associated with other clinical variables in this analysis after adjusting for 25 tests. Of note, the variant was not associated with the development of insomnia in the survival analysis. This could be due to low power of the analysis (N=1,112) or the variant may be important for the development of insomnia in an earlier phase of the disease.

Targeted assessment for the PD risk variants

Of the 90 risk variants from the recently published PD GWAS, rs34637584 (*LRRK2* p.G2019S) and rs76763715 (*GBA* p.N370S) were not available in the meta-analyses because of their minor allele frequency (MAF) < 0.01. The remaining 88 PD GWAS risk SNPs were assessed in our 25 GWAS summary sets, resulting in evaluations of 2022 candidate associations. 112 associations between known genetic risk variants and clinical markers had raw p-values less than 0.05. After Bonferroni correction for all evaluated candidate associations, nine surpassed the threshold of the analyses-wide significance for the maximum of 25 analyses per variant (raw P-value < 0.002). The directions of these associations generally indicated that having the higher risk allele was associated with more severe deficits in both the cognitive and motor domains of PD, but not for sleeping problems. Having the risk allele (A) of rs1293298 (intron variant of *CTSB*) was associated with a lower risk of developing insomnia (HR 0.79 [0.69, 0.91], P-value = 1.2E-3), and the risk allele (A) of rs6500328 (intron variant of *NOD2*) and (A) of rs76116224 (intergenic variant close to 3' end of *KCNS3*) were associated with a lower prevalence of daytime sleepiness at baseline (OR 0.76 [0.64, 0.90], P-value = 1.4E-3; OR 0.47 [0.32, 0.68], P-value = 8.4E-5; respectively). Among the nine associations with analysis-wide significance, three were significant after adjusting for 88 variants (raw P-value < 5.68E-4), and one among them had test-wide significance (raw P-value < 2.47E-5). Figure 3 shows the strength of the associations for the selected variants with associations of analyses-wide significance in at least one analysis. This figure suggests that some risk variants were associated with specific clinical features. For example, rs35749011 was associated with both the HR of cognitive

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impairment at test-wide significance (HR 2.45 [1.64, 3.65] for the minor allele, P-value = 1.1E-5) and lower MoCA score over time at analyses-wide significance (-1.16 [-1.89, -0.43], P-value = 0.0018). Although it is an intergenic variant whose closest gene is *KRTCAP2*, the variant is in high LD ($r^2 = 0.78$) with rs2230288 (*GBA* p.E365K),^{18,19} and has a similar spectrum of phenotype associations as rs2230288. Other notable variants with variant-wide significance were rs76904798, the intergenic variant close to the 5' end of *LRRK2*, for reaching HY3 (HR 1.32 [1.14, 1.54] with the minor allele of T, P-value = 3.0E-4), and rs76116224 and the baseline OR of having daytime sleepiness mentioned above. The detailed information for all of the test results is provided as supplemental material. (Supplemental Table 4 and Supplemental Figure 2)

***GBA* protein coding variants and APOE tagging variants**

In the focused analyses for *GBA* coding variants, rs75548401, *GBA* p.T408M, was associated with the faster development of HY3 (HR 2.35 [1.58, 3.49], P-value = 2.5E-5). rs2230288, *GBA* p.E365K, was associated with the higher odds of having cognitive impairment at baseline (OR 2.05 [1.33, 3.18], P-value = 1.3E-3), faster development of cognitive impairment (HR 2.58 [1.71, 3.89] P-value = 5.5E-6), and lower MoCA score at the analysis-wide significance (Beta -1.23 [-1.97, -0.50], P-value = 1.0E-3). We previously reported these associations²⁰ and we were able to confirm them in our updated analysis with more stringent multiple testing correction (FDR vs Bonferroni).

The C allele of rs429358, the tagging variant for the *APOE* E4 allele, was associated with lower MMSE (Beta -0.20 [-0.33, -0.07], P-value = 2.8E-3) and lower MoCA (Beta -0.52 [-0.86, -0.17], P-value = 3.4E-3) as expected. Moreover, it was associated with higher UPDRS part 1 scores (Beta 0.12 [0.04, 0.20] in Z score, P-value = 4.5E-3). We did not have enough evidence to conclude that the *APOE* E4 allele was associated with the prevalence of cognitive impairment at baseline (P-value = 0.4) or its development during follow-ups (P-value = 0.034). The T allele of rs7412 showed no association with these measurements, also predicted as this variant tagging *APOE* E2.

Discussion

We conducted GWAS using longitudinal data from multiple PD cohorts to investigate markers of PD progression and heterogeneity. Of the 25 meta-analyses that we evaluated, we identified two variant-phenotype associations with genome-wide significance.

We also evaluated the summary statistics to assess clinical value of the variants of interest.

One of our genome-wide hits, rs382940, in the intron of *SLC44A1*, was associated with a faster rate of progression to reach HY3. *SLC44A1*, soluble carrier 44A1, is also referred to as choline transporter-like protein 1 (CTL1). The gene is ubiquitously expressed in the brain, colon, thyroid and other organs and is involved in choline transport. No associations with PD and this variant or the gene itself have been reported so far although it has been studied in several vitro and vivo studies.^{21–24} Further investigation is warranted. The search of the Brain eQTL database suggested that another GWAS-signal, rs61863020, was associated with *ADRA2A* expression, a gene reported to be associated with arousal/sleep state.²⁵ *ADRA2A* is consistently expressed in locus coeruleus as well as nigral dopamine neurons and pyramidal neurons of the human brain (<http://www.humanbraincode.org/>).²⁶ The *ADRA2A*-encoded alpha2 adrenoreceptor modulates norepinephrine levels. In addition, norepinephrine²⁷ and its receptors^{28,29} have been linked to PD in multiple model systems.

Interestingly, neither of the variants were reported to be associated with the incidence of Parkinson's disease in the recent case-control analysis of PD.³ A case-control study cannot address some mechanisms which contribute to the heterogeneity of PD such as genetic effects only relevant to cases or interactions with PD treatments. The discrepancy between the case-control GWAS and our study may reflect this point.

In the targeted assessments, we confirmed the previous results of the associations between *GBA* risk variants and motor and cognitive aspects of PD.^{30–34} In contrast with *GBA* variants, association studies of *APOE* and cognitive function in PD have yielded mixed results previously.^{35–39} Our data supported the association of *APOE* and cognitive function on two measurements; MMSE and MoCA.

The strength of the current study is the hypothesis-free approach of GWAS, which can be powerful in identifying new associations and expanding our biological knowledge-base.

While the associations here should be replicated and further investigated with vivo/vitro experiments, these findings suggest the prioritization of the two variants and loci for future validations. We have reported all of the summary results on our publicly accessible site to

benefit researchers so that they may conduct/replicate the analysis of variants of interest in their own research.

The major limitation of this study is the heterogeneity of the cohorts, which is apparent in several ways: baseline characteristics, definitions of binomial outcomes, patterns for clinical care over the course of follow-up, the platforms for genotyping/sequencing, and sample acquisition/enrollment practices. By meta-analyzing at the dataset-level and exercising careful quality control throughout, we tried to extract the most generalizable and reliable results across cohorts.

Another limitation is the power of the study. Although we have aggregated the largest collection of longitudinal data in PD genetics so far, more data would be needed to identify relatively small differences expected within PD patients compared to the case-vs-control setting. From the meta-analysis results, we estimated that if we had 30% more participants in the same setting, we would have had at least one variant of the genome-wide significance ($5E-8$) in 21 out of 25 phenotypes (Supplemental Table 5). Additionally, our study results can be a valuable resource for validation and hypothesis testing as we have shown in our targeted analysis. The study website aims to provide other researchers with a tool to explore variants of their interest easily for all included phenotypes.

(<https://pdgenetics.shinyapps.io/pdprogmetagwasbrowser/>)

In our survival analysis, we did not explicitly check the proportional hazard assumption. If a variant effect changed over time, the result would be interpreted as the average HR over time. Also, the result would be biased when one of the covariates violated the proportional hazard assumption in our model and it was also associated with the variant dosage. Replication is important in this regard as well.

Finally, the study participants were restricted to individuals with European ancestry. We are now striving to collect more data, including from populations that are under-represented in this study, to improve our understanding of this topic in future studies.

Conclusion

With 4,093 participants and 22,307 longitudinal data points over a median of 3.81 years, we performed 25 GWAS meta-analyses. We found two genome-wide significant signals: the rate to reach HY3 during the disease course and rs382940; and the prevalence of insomnia at baseline and rs61863020. We also conducted targeted assessments of previously published

variants of interest using the GWAS results. These results provide valuable insights into how genetic factors contribute to the heterogeneity of PD and disease progression.

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Supplementary Materials

- Appendix: The description of study cohorts (A). IPDGC collaborators (B)
- Supplemental table 1: Cohort specific definitions of binomial outcomes
- Supplemental table 2: Analytical models per datasets
- Supplemental table 3: The study-specific genomic inflation factors
- Supplemental table 4: The meta-analysis results of the association between risk variants and the clinical features and progression of Parkinson’s disease
- Supplemental table 5: The estimated study size to detect at least one variant with genome-wide significance
- Supplemental figure 1: Gene-based test for reaching Hoehn and Yahr stage 3 or higher
- Supplemental figure 2: Heatmap for the meta-analysis results of the association between risk variants and the clinical features and progression of Parkinson’s disease

References

1. Postuma RB, Berg D, Stern M, et al. MDS clinical diagnostic criteria for Parkinson’s disease. *Mov Disord.* 2015;30:1591–1601.

2. Keller MF, Saad M, Bras J, et al. Using genome-wide complex trait analysis to quantify “missing heritability” in Parkinson’s disease. *Hum Mol Genet.* 2012;21:4996–5009.

3. Nalls MA, Blauwendraat C, Vallerga CL, et al. Expanding Parkinson’s disease genetics: novel risk loci, genomic context, causal insights and heritable risk. *bioRxiv.* Epub 2019.

4. Leonard H, Blauwendraat C, Krohn L, et al. Genetic variability and potential effects on clinical trial outcomes: perspectives in Parkinson’s disease. *bioRxiv* 2018.

5. Goetz CG, Poewe W, Rascol O, et al. Movement Disorder Society Task Force report on the Hoehn and Yahr staging scale: Status and recommendations The Movement Disorder Society Task Force on rating scales for Parkinson’s disease. *Mov Disord.* 2004;19:1020–1028.

6. Goetz CG, Fahn S, Martinez-Martin P, et al. Movement Disorder Society-sponsored revision of the Unified Parkinson’s Disease Rating Scale (MDS-UPDRS): Process,

- format, and clinimetric testing plan. *Mov Disord*. 2007;22:41–47.
7. Nasreddine ZS, Phillips NA, Bédirian V, et al. The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. *J Am Geriatr Soc*. 2005;53:695–699.
 8. Nalls MA, Bras J, Hernandez DG, et al. NeuroX, a fast and efficient genotyping platform for investigation of neurodegenerative diseases. *Neurobiol Aging*. 2015;36:1605.e7-1605.e12.
 9. Purcell S, Neale B, Todd-Brown K, et al. PLINK: A Tool Set for Whole-Genome Association and Population-Based Linkage Analyses. *Am J Hum Genet*. 2007;81:559–575.
 10. Das S, Forer L, Schön herr S, et al. Next-generation genotype imputation service and methods. *Nat Genet*. 2016;48:1284–1287.
 11. Zhan X, Hu Y, Li B, Abecasis GR, Liu DJ. RVTESTS: an efficient and comprehensive tool for rare variant association analysis using sequence data: Table 1. *Bioinformatics*. 2016;32:1423–1426.
 12. Sä fken B, Rügamer D, Kneib T, Greven S. Conditional Model Selection in Mixed-Effects Models with cAIC4. Epub 2018 Mar 15.
 13. Willer CJ, Li Y, Abecasis GR. METAL: fast and efficient meta-analysis of genomewide association scans. *Bioinformatics*. 2010;26:2190–2191.
 14. Pruim RJ, Welch RP, Sanna S, et al. LocusZoom: regional visualization of genome-wide association scan results. *Bioinformatics*. 2010;26:2336–2337.
 15. Watanabe K, Taskesen E, van Bochoven A, Posthuma D. Functional mapping and annotation of genetic associations with FUMA. *Nat Commun*. 2017;8:1826.
 16. Vösa U, Claringbould P, Westra H-J, et al. Unraveling the polygenic architecture of complex traits using blood eQTL meta-analysis. *bioRxiv*. Epub 2018.
 17. Qi T, Wu Y, Zeng J, et al. Identifying gene targets for brain-related traits using transcriptomic and methylomic data from blood. *Nat Commun*. 2018;9:2282.
 18. Berge-Seidl V, Pihlström L, Maple-Grødem J, et al. The GBA variant E326K is associated with Parkinson's disease and explains a genome-wide association signal. *Neurosci Lett*. 2017;658:48–52.

19. Blauwendraat C, Bras JM, Nalls MA, Lewis PA, Hernandez DG, Singleton AB. Coding variation in GBA explains the majority of the SYT11-GBA Parkinson's disease GWAS locus. *Mov Disord*. 2018;33:1821–1823.
20. Iwaki H, Blauwendraat C, Leonard HL, et al. Genetic risk of Parkinson disease and progression: *Neurol Genet*. 2019;5:e348.
21. Machová E, O'Regan S, Newcombe J, et al. Detection of choline transporter-like 1 protein CTL1 in neuroblastoma × glioma cells and in the CNS, and its role in choline uptake. *J Neurochem*. Wiley Online Library; 2009;110:1297–1309.
22. Schenkel LC, Singh RK, Michel V, et al. Mechanism of choline deficiency and membrane alteration in postural orthostatic tachycardia syndrome primary skin fibroblasts. *FASEB J*. 2015;29:1663–1675.
23. Heffernan C, Jain MR, Liu T, et al. Nectin-like 4 Complexes with Choline Transporter-like Protein-1 and Regulates Schwann Cell Choline Homeostasis and Lipid Biogenesis in Vitro. *J Biol Chem*. 2017;292:4484–4498.
24. Gao P, He M, Zhang C, Geng C. Integrated analysis of gene expression signatures associated with colon cancer from three datasets. *Gene*. 2018;654:95–102.
25. Gelegen C, Gent TC, Ferretti V, et al. Staying awake - a genetic region that hinders α 2 adrenergic receptor agonist-induced sleep. *Eur J Neurosci*. 2014;40:2311–2319.
26. Dong X, Liao Z, Gritsch D, et al. Enhancers active in dopamine neurons are a primary link between genetic variation and neuropsychiatric disease. *Nat Neurosci*. 2018;21:1482–1492.
27. Tong J, Hornykiewicz O, Kish SJ. Inverse Relationship Between Brain Noradrenaline Level and Dopamine Loss in Parkinson Disease. *Arch Neurol*. 2006;63:1724.
28. Srinivasan J, Schmidt WJ. Treatment with α 2-adrenoceptor antagonist, 2-methoxy idazoxan, protects 6-hydroxydopamine-induced Parkinsonian symptoms in rats: neurochemical and behavioral evidence. *Behav Brain Res*. 2004;154:353–363.
29. Mittal S, Bjørnevik K, Im DS, et al. β 2-Adrenoreceptor is a regulator of the α -synuclein gene driving risk of Parkinson's disease. *Science (80-)*. 2017;357:891–898.
30. Winder-Rhodes SE, Evans JR, Ban M, et al. Glucocerebrosidase mutations influence the natural history of Parkinson's disease in a community-based incident cohort. *Brain*.

- 2013;136:392–399.
31. Brockmann K, Srulijes K, Pflederer S, et al. GBA -associated Parkinson's disease: Reduced survival and more rapid progression in a prospective longitudinal study. *Mov Disord.* 2015;30:407–411.
 32. Davis AA, Andruska KM, Benitez BA, Racette BA, Perlmutter JS, Cruchaga C. Variants in GBA , SNCA , and MAPT influence Parkinson disease risk, age at onset, and progression. *Neurobiol Aging.* 2016;37:209.e1-209.e7.
 33. Davis MY, Johnson CO, Leverenz JB, et al. Association of GBA Mutations and the E326K Polymorphism With Motor and Cognitive Progression in Parkinson Disease. *JAMA Neurol.* 2016;73:1217.
 34. Liu G, Boot B, Locascio JJ, et al. Specifically neuropathic Gaucher's mutations accelerate cognitive decline in Parkinson's. *Ann Neurol.* 2016;80:674–685.
 35. Huang X, Chen P, Kaufer DI, Tröster AI, Poole C. Apolipoprotein E and Dementia in Parkinson Disease. *Arch Neurol.* 2006;63:189.
 36. Kurz MW, Dekomien G, Nilsen OB, Larsen JP, Aarsland D, Alves G. APOE Alleles in Parkinson Disease and Their Relationship to Cognitive Decline: A Population-based, Longitudinal Study. *J Geriatr Psychiatry Neurol.* SAGE Publications Inc STM; 2009;22:166–170.
 37. Federoff M, Jimenez-Rolando B, Nalls MA, Singleton AB. A large study reveals no association between APOE and Parkinson's disease. *Neurobiol Dis.* 2012;46:389–392.
 38. Mata IF, Leverenz JB, Weintraub D, et al. APOE , MAPT , and SNCA Genes and Cognitive Performance in Parkinson Disease. *JAMA Neurol.* 2014;71:1405.
 39. Paul KC, Rausch R, Creek MM, et al. APOE, MAPT, and COMT and Parkinson's Disease Susceptibility and Cognitive Symptom Progression. *J Parkinsons Dis.* 2016;6:349–359.

Figure legends

Figure 1: Graphical overview of the analysis strategy.

* DIGPD cohort was analyzed separately depending on the genotyping system.

Rsq, R square; MAF, Minor allele frequency; HWE, Hardy–Weinberg equilibrium test; OR, Odds ratio; HR, Hazard ratio; PC, Principal components; AAD, Age at diagnosis; YfD, Years from diagnosis to observation; HY score, the score on the Hoehn and Yahr scale;

Figure 2: Locuszoom plots and forest plots of the two genome-wide significant hits. A: The locus plot for rs382940 which is associated with HY3. B: The locus plot for rs61863020 which is associated with insomnia. C: The forest plot for rs382940. D: The forest plot for rs61863020.

Figure 3: Heatmap of the Parkinson's disease GWAS loci associated with progression markers

Cream, P-value > 0.05; light green, P-value < 0.05; green: P-value < 0.002; blue, P-value < 5.68E-4; dark blue, P-value < 2.47E-5).

CONST, constipation; COGi, cognitive impairment; DEPR, depression; HY3, Hoehn and Yahr score; INS, insomnia; MMSE, Mini-Mental State Examination; MOCA, Montreal Cognitive Assessment; SEADL70, the modified Schwab and England Activities of Daily Living Scale; SLEEP, daytime sleepiness; UPDRS, Unified Parkinson's Disease Rating Scale (UPDRS) or the Movement Disorder Society revised UPDRS, scaled at the baseline (UPDRS1-3) or during the course.

Suffix of 'base' indicates the logistic regression model at baseline, 'surv' for the survival analysis over the course, and 'cont' for the linear mixed effect model for continuous outcome analyzed by linear mixed model.

Figure 4: Heatmap of the GBA and APOE variants associated with progression markers

Cream, P-value > 0.05; light green, P-value < 0.05; green: Bonferroni corrected P-value < 0.05;

CONST, constipation; COGi, cognitive impairment; DEPR, depression; HY3, Hoehn and Yahr score; INS, insomnia; MMSE, Mini-Mental State Examination; MOCA, Montreal Cognitive Assessment; SEADL, the modified Schwab and England Activities of Daily Living Scale; SLEEP, daytime sleepiness; UPDRS, Unified Parkinson's Disease Rating Scale (UPDRS) or the Movement Disorder Society revised UPDRS, scaled at the baseline (UPDRS1-3) or during the course.

Suffix of 'base' indicates the logistic regression model at baseline, 'surv' for the survival

analysis over the course, and ‘cont’ for the linear mixed effect model for continuous outcome analyzed by linear mixed model.

Author Roles

1. Research project: A. Conception, B. Organization, C. Execution; 2. Statistical Analysis: A. Design, B. Execution, C. Review and Critique; 3. Manuscript Preparation: A. Writing of the first draft, B. Review and Critique;

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GWAS of Parkinson’s disease clinical biomarkers in 12 longitudinal patients’ cohorts

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Abstract

Background: Several reports have identified different patterns of Parkinson's disease progression in individuals carrying missense variants in *GBA* or *LRRK2* genes. The overall contribution of genetic factors to the severity and progression of Parkinson's disease, however, has not been well studied.

Objectives: To test the association between genetic variants and the clinical features ~~and progression~~ of Parkinson's disease on a genome-wide scale.

Methods: We accumulated individual data from 12 longitudinal cohorts in a total of 4,093 patients with 22,307 observations over a median of 3.81 years. Genome-wide associations were evaluated for 25 cross-sectional and longitudinal phenotypes. Specific variants of interest, including 90 recently-identified disease risk variants, were also investigated post-hoc for candidate associations with these phenotypes.

Results: Two variants were genome-wide significant. Rs382940(T>A), within the intron of *SLC44A1*, was associated with reaching Hoehn and Yahr stage 3 or higher faster (HR 2.04 [1.58, 2.62], P-value = 3.46E-8). Rs61863020(G>A), an intergenic variant and eQTL for *ADRA2A*, was associated with a lower prevalence of insomnia at baseline (OR 0.63 [0.52, 0.75], P-value = 4.74E-8). In the targeted analysis, we found nine associations between known Parkinson's risk variants and more severe motor/cognitive symptoms. Also, we replicated previous reports of *GBA* coding variants (rs2230288: p.E365K, rs75548401: p.T408M) being associated with greater motor and cognitive decline over time, and *APOE* E4 tagging variant (rs429358) being associated with greater cognitive deficits in patients.

Conclusions: We identified novel genetic factors associated with heterogeneity of Parkinson's disease. The results can be used for validation or hypothesis tests regarding ~~provide new insights into the pathogenesis of~~ Parkinson's disease.

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Main text:

Introduction

Parkinson’s disease (PD) is clinically defined by its motor features of rigidity, bradykinesia, gait disturbance, and tremor. Although these prominent features are important for diagnosis, patients with PD also suffer from many non-motor features such as constipation, urinary incontinence, orthostatic hypotension, REM sleep behavior disorder (RBD), apathy, hyposmia, and cognitive impairment.¹ Moreover, patients develop motor complications, including wearing off and dyskinesia, as side effects of medication. The onset, intensity and progression of these different PD clinical features vary among individuals, and the mechanisms underlying this heterogeneity are not well understood.

Recent genome-wide studies have identified 90 common variants associated with the risk of PD, with an overall heritability estimated to be between 22-27%.^{2,3} While previous studies have indicated the importance of genetic contributions to disease risk, the contribution of genetic factors to PD progression and heterogeneity has not been well studied. Investigating genetic factors associated with disease progression and heterogeneity in disease presentation is an important step in elucidating the underlying molecular mechanisms and identifying better patient stratification in clinical trials.⁴

Longitudinal patient cohorts are powerful resources that can be used to explore the impact of genetics on the trajectory of PD-related phenotypes; the inherent precision of repeated measurements over time provides more power to detect these associations. However, the available number of participants in each study is usually not enough to conduct a genome-wide association study (GWAS). In this study, we accumulated 22,307 follow-up visits from 4,093 patients across 12 cohorts (Table 1) and performed meta-analyses of longitudinal GWAS on the progression markers of Parkinson’s disease. Using the results from this meta-analysis, we evaluated how known risk variants, including the 90 recently identified variants for PD,³ *GBA* protein coding mutations, and *APOE* tagging variants were associated with the progression of phenotypes. To maximize the utility of this work to other researchers, we have made all results from this study publicly searchable and available for download.

[\(https://pdgenetics.shinyapps.io/pdprogmetagwasbrowser/\)](https://pdgenetics.shinyapps.io/pdprogmetagwasbrowser/)

Methods

Cohorts

Twelve longitudinal cohorts of PD patients recruited across North America, Europe and Australia were included in our study. The following observational studies were included: the Drug Interaction with Genes in Parkinson's Disease (DIGPD), the Harvard Biomarkers Study (HBS), the Oslo Parkinson's Disease study (partly including retrospective data), the Norwegian ParkWest study (PARKWEST), the Parkinson's Disease Biomarker Program (PDBP), the Parkinsonism Incidence and Cognitive and Non-motor heterogeneity In Cambridgeshire (PICNICS), the Parkinson's Progression Markers Initiative (PPMI), and the Profiling Parkinson's disease study (PROPARK). The four cohorts included were randomized clinical trials: the Deprenyl and Tocopherol Antioxidative Therapy of Parkinsonism (DATATOP), the NIH Exploratory Trials in Parkinson's Disease Large Simple Study 1 (NET-PD_LS1), the ParkFit study (PARKFIT), and the Parkinson Research Examination of CEP-1347 Trial study with its subsequent prospective study (PreCEPT/PostCEPT). More details of these cohorts are described in Appendix. Participants' information and genetic samples were obtained under appropriate written consent and with local institutional and ethical approvals.

Phenotyping

Each cohort had a different set of recorded biomarkers and phenotypes associated with Parkinson's disease. We selected the following continuous and binomial biomarkers based on their clinical importance and availability. For continuous outcomes, we collected the scores of Hoehn and Yahr staging scale (HY),⁵ total and sub-scores of the Unified Parkinson's Disease Rating Scale (UPDRS) or the Movement Disorder Society revised UPDRS version (MDS-UPDRS),⁶ Mini-Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA)⁷ and the modified Schwab and England Activities of Daily Living Scale (SEADL). With the exception of the subscores of UPDRS/MDS-UPDRS part 4, total scores and the subscores of UPDRS and MDS-UPDRS were normalized to the population-baseline mean and standard deviation and converted to Z values. The subscores of UPDRS/MDS-UPDRS part 4, measuring complication of treatment, were normalized to the mean and standard deviation of all observations because the score was 0 at the baseline for the de-novo PD

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cohorts. We also determined whether subjects were recorded as presenting the following binomial outcomes during participant visits: constipation, cognitive impairment, depression, daytime sleepiness, Hoehn and Yahr stage of 3 or worse (HY3), hyposmia, insomnia, motor fluctuation, REM sleep behavior disorder (RBD), restless legs syndrome (RLS), and an SEADL of 70 or less (SEADL70). Because study-specific criteria for these binomial outcomes were not consistent amongst the studies, we tried to use the common criteria for these binomial outcomes if we had access to the raw data from the studies. The details of the definitions of binomial outcomes are provided in the Supplemental Table 1.

Genetics data

The genotyping was conducted with NeuroX, a targeted chip for neurodegenerative disease,⁸ for NET-PD_LS1, a part of DIGPD (DIGPD_neuroX), HBS, PDBP, and PRECEPT. The rest of DIGPD (DIGPD_chip) were genotyped using Illumina Multi-Ethnic Genotyping Array. Participants in DATATOP, OSLO, PARKFIT, PARKWEST, PICNICS, and PROPARK were genotyped using Illumina Infinium OmniExpress array. Whole genome sequencing data was used for PPMI, with the detailed methods for genome sequencing provided on the PPMI website (<https://www.ppmi-info.org/>).

Variant inclusion criteria consisted of call rate > 0.95, MAF > 0.01, and Hardy-Weinberg equilibrium test statistic > 1E-4. Participants were excluded due to the following criteria: high-missingness (> 5% for genotyped variants), sex discordance, extreme heterozygosity (F statistics > 0.15), Non-European ancestry confirmed by joint analysis with HapMap 3 data using principal component (Outside of mean +/- 6 SD in PC1 or PC2 for European reference samples) (International HapMap 3 Consortium et al., 2010), and excessive relatedness (pairwise kinships > 0.125). We used PLINK version 1.9 for the above filtering.⁹

For all samples and variants passing quality control, imputation was conducted for chromosome 1 to 22 using Minimac3 using the Haplotype Reference Consortium panel (HRC r1.1) and Eagle v2.3 for phasing at the Michigan Imputation Server¹⁰, with the exception of the whole genome sequenced PPMI dataset. SNPs with an imputation quality of R2 less than 0.3 and MAF < 1% were excluded. After quality control, the number of variants were approximately 2.6 - 2.9 million in NET-PD_LS1, DIGPD_neuroX, HBS, PDBP, and PRECEPT; 7.7 - 7.8 million in PICNICS, PROPARK, PARKWEST, DATATOP, PARKFIT,

DIGPD, and OSLO; and 8.6 million in PPMI. Note that the cohorts genotyped by NeuroX had relatively less genome coverage than others.

Cohort-level analyses

We conducted a separate GWAS for each cohort per phenotype of interest. In addition, DIGPD cohorts were analyzed separately according to the genotyping array used (DIGPD_neuroX cohort and DIGPD_chip cohort). Each outcome was analyzed by an additive model with covariates. For the binomial outcomes at baseline visit, when the outcomes were positive for more than 5% of participants and >20 counts, logistic regression analyses were conducted. Those without the binomial outcome at baseline were followed-up until either censored or the development of the outcome. If more than 20 events were observed during follow-ups, the outcome was analyzed using cox proportional hazard models with time-varying covariates. For the analysis of continuous traits, linear mixed models were used to evaluate the variants' association for the outcome. Age at diagnosis, year from diagnosis to the observation, and sex were adjusted for in all analyses. In addition, the following covariates were associated with the outcome of interest in a backwards stepwise manner: quadratic age, quadratic years from diagnosis, years of education, medication status (levodopa usage, dopamine agonist usage, using either dopamine agonist or levodopa), and a Hoehn and Yahr score of 2 or more at the first observation (except for the models regressing for Hoehn and Yahr score itself or UPDRS motor score). These covariates were selected per study using Akaike's Information Criteria (AIC) for logistic models and Cox survival models, and conditional AIC (cAIC) for linear mixed effect models. The cohort level analyses were conducted with R (version 3.5.0 <https://www.r-project.org/>) and rvttests.¹¹ R package 'cAIC4' was used to calculate cAIC.¹²

Meta-Analyses

The results from cohort-level analyses were combined using an inverse variance weighted fixed effect model. If the study-specific genomic inflation factor was more than 1.2, the study was excluded from the meta-analysis. Five of the 204 GWAS were excluded based on these criteria. For other cohorts, the overall alpha error was corrected using the genomic inflation factor before the meta-analysis. Meta-analyses were carried out with METAL.¹³ From the

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meta-analysis results, we only evaluated variants with $MAF > 0.05$ due to statistical power constraints. We also excluded variants with minor allele frequency variability greater than 15% across cohorts. Further exclusions at the meta-analysis level include variants with Cochran's Q-test for heterogeneity < 0.05 and a total participant $N < 1000$. The null hypothesis was tested with a significance level of $5E-8$ on a two-sided test. For genome-wide signals, additional visualization and functional analyses were conducted using LocusZoom,¹⁴ FUMA (<http://fuma.ctglab.nl/snp2gene/>, version 1.3.3d).¹⁵ FUMA is a web-based annotation tool using MAGMA to conduct gene-based tests, a gene-set analysis and a tissue expression analysis. We applied a default setting. Also, we explored in eQTLGen database (<http://www.eqtlgen.org/>)¹⁶ and meta-analyzed expression data in the brain accessible from the study by Qi et al.¹⁷

Associations with the variants of interest, including the recently identified 90 risk variants for PD, known *LRRK2* and *GBA* variants, and *APOE*, were extracted from the meta-analysis results. We exploratory evaluated the associations of these variants and clinical features based on the significance level of 0.05, applying the Bonferroni adjustment of a maximum of 25 tests per variant (raw P-value < 0.002).

The summary of analytical processes is shown in figure 1.

Data availability

The summary statistics of the meta-analysis results, including the ones which were not evaluated in this manuscript, are publicly available for convenient browsing and downloading. (<https://pdgenetics.shinyapps.io/pdprogmetagwasbrowser/>)

Results

Novel GWAS associations with PD progression markers

The cohort characteristics are provided in Table 1. Overall, we analyzed 4,093 participants with 22,307 longitudinal data points over a median of 3.81 years. These cohorts varied in the years between enrollment and diagnosis, as well as follow-up durations. DATATOP,

ParkWest, PPMI, and PreCEPT/PostCEPT enrolled untreated PD patients while others enrolled both treated and untreated patients. Considering the difference in design and recruitment strategies in the cohorts (Appendix), it is important to adjust for baseline characteristics as well as the follow-up lengths per cohort-level. All cohort-specific models for analysis are listed in Supplemental Table 2.

In total, 204 GWAS were conducted and combined into 33 meta-analyses. Eight meta-analyses were not evaluated because of the small number of total participants in the analyses (N total <1000). Those excluded were baseline analyses for RBD, RLS and SEADL70; and longitudinal analyses for constipation, daytime sleepiness, hyposmia, RBD, and RLS. Therefore, we investigated 9 binomial traits at baseline, 7 binomial traits for survival, and 9 continuous traits over the follow-ups. The genomic inflation factor was the mean value of 0.993, SD of 0.023, and the range was [0.951, 1.031] across meta-analyses. The study specific genomic inflation factors were provided in Supplemental Table 3.

One association with the progression of PD was of genome-wide significance (P-value < 5.00E-08). The minor allele of rs382940 (chr9:108058562T>A), an intronic variant of *SLC44A1*, was associated with a higher hazard ratio (HR) of reaching Hoehn and Yahr stage 3.0 or greater (HR 2.04 [1.58, 2.62], P-value = 3.46E-8 (Estimates in a random effect model, 1.97 [1.38, 2.81], P-value = 1.96E-4)). When considering the baseline observations, the minor allele of rs61863020 (chr10:112956055G>A), an intergenic variant, was significantly associated with the lower baseline OR of having insomnia (OR 0.63 [0.52, 0.75], P-value = 4.74E-8 (The same estimates and P-value in a random effect model)). Locus plots and forest plots for these two associations are shown in Figure 2. Cochran's Q statistics, I-square and forest plots all showed no evidence of heterogeneity for these associations. (Figure 2)

To evaluate the potential molecular mechanism for the two genome-wide signals, we explored eQTL datasets in blood and brain,^{16,17} and functional annotation of the GWAS summary statistics using FUMA. Although it is in a regulatory region of *SLC44A1*, rs382940 itself was not reported to be an eQTL in blood or brain. Gene-based tests using the GWAS summary statistics for reaching HY3 showed that *SLC44A1* was significant gene-wise (P-value = 5.8E-07 < Bonferroni correction threshold = 2.7E-6, supplemental figure 1).

Rs61863020 was a significant eQTL for *ADRA2A* (α -2A adrenergic receptor) (P-value = 7.2E-4, the Bonferroni corrected P-value = 6.5E-3, up-regulation for A allele) in the brain.

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In the meta-analysis results from the other clinical outcomes, rs382940 was associated with higher scores in the UPDRS part 2 and part 3 (UPDRS2_scaled: 0.36 [0.15, 0.57], P-value = 8.21E-04; UPDRS3_scaled: 0.29 [0.14, 0.45], P-value = 2.18E-04). These findings are consistent with the primary association of rs382940 and reaching HY3, which is a significant motor milestone (bilateral signs on clinical examination and the emergence of postural instability). Except for the association with having insomnia at baseline, rs61863020 was not significantly associated with other clinical variables in this analysis after adjusting for 25 tests. Of note, the variant was not associated with the development of insomnia in the survival analysis. This could be due to low power of the analysis (N=1,112) or the variant may be important for the development of insomnia in an earlier phase of the disease.

Targeted assessment for the PD risk variants

Of the 90 risk variants from the recently published PD GWAS, rs34637584 (*LRRK2* p.G2019S) and rs76763715 (*GBA* p.N370S) were not available in the meta-analyses because of their minor allele frequency (MAF) < 0.01. The remaining 88 PD GWAS risk SNPs were assessed in our 25 GWAS summary sets, resulting in evaluations of 2022 candidate associations. 112 associations between known genetic risk variants and clinical markers had raw p-values less than 0.05. After Bonferroni correction for all evaluated candidate associations, nine surpassed the threshold of the analyses-wide significance for the maximum of 25 analyses per variant (raw P-value < 0.002). The directions of these associations generally indicated that having the higher risk allele was associated with more severe deficits in both the cognitive and motor domains of PD, but not for sleeping problems. Having the risk allele (A) of rs1293298 (intron variant of *CTSB*) was associated with a lower risk of developing insomnia (HR 0.79 [0.69, 0.91], P-value = 1.2E-3), and the risk allele (A) of rs6500328 (intron variant of *NOD2*) and (A) of rs76116224 (intergenic variant close to 3' end of *KCNS3*) were associated with a lower prevalence of daytime sleepiness at baseline (OR 0.76 [0.64, 0.90], P-value = 1.4E-3; OR 0.47 [0.32, 0.68], P-value = 8.4E-5; respectively). Among the nine associations with analysis-wide significance, three were significant after adjusting for 88 variants (raw P-value < 5.68E-4), and one among them had test-wide significance (raw P-value < 2.47E-5). Figure 3 shows the strength of the associations for the selected variants with associations of analyses-wide significance in at least one analysis. This figure suggests that some risk variants were associated with specific clinical features. For example, rs35749011 was associated with both the HR of cognitive

impairment at test-wide significance (HR 2.45 [1.64, 3.65] for the minor allele, P-value = 1.1E-5) and lower MoCA score over time at analyses-wide significance (-1.16 [-1.89, -0.43], P-value = 0.0018). Although it is an intergenic variant whose closest gene is *KRTCAP2*, the variant is in high LD ($r^2 = 0.78$) with rs2230288 (*GBA* p.E365K),^{18,19} and has a similar spectrum of phenotype associations as rs2230288. Other notable variants with variant-wide significance were rs76904798, the intergenic variant close to the 5' end of *LRRK2*, for reaching HY3 (HR 1.32 [1.14, 1.54] with the minor allele of T, P-value = 3.0E-4), and rs76116224 and the baseline OR of having daytime sleepiness mentioned above. The detailed information for all of the test results is provided as supplemental material. (Supplemental Table 4 and Supplemental Figure 2)

***GBA* protein coding variants and APOE tagging variants**

In the focused analyses for *GBA* coding variants, rs75548401, *GBA* p.T408M, was associated with the faster development of HY3 (HR 2.35 [1.58, 3.49], P-value = 2.5E-5). rs2230288, *GBA* p.E365K, was associated with the higher odds of having cognitive impairment at baseline (OR 2.05 [1.33, 3.18], P-value = 1.3E-3), faster development of cognitive impairment (HR 2.58 [1.71, 3.89] P-value = 5.5E-6), and lower MoCA score at the analysis-wide significance (Beta -1.23 [-1.97, -0.50], P-value = 1.0E-3). We previously reported these associations²⁰ ~~(in press at *Neurology Genetics*)~~ and we were able to confirm them in our updated analysis with more stringent multiple testing correction (FDR vs Bonferroni). The C allele of rs429358, the tagging variant for the *APOE* E4 allele, was associated with lower MMSE (Beta -0.20 [-0.33, -0.07], P-value = 2.8E-3) and lower MoCA (Beta -0.52 [-0.86, -0.17], P-value = 3.4E-3) as expected. Moreover, it was associated with higher UPDRS part 1 scores (Beta 0.12 [0.04, 0.20] in Z score, P-value = 4.5E-3). We did not have enough evidence to conclude that the *APOE* E4 allele was associated with the prevalence of cognitive impairment at baseline (P-value = 0.4) or its development during follow-ups (P-value = 0.034). The T allele of rs7412 showed no association with these measurements, also predicted as this variant tagging *APOE* E2.

Discussion

We conducted GWAS using longitudinal data from multiple PD cohorts to investigate markers of PD progression and heterogeneity. Of the 25 meta-analyses that we evaluated, we identified two variant-phenotype associations with genome-wide significance.

We also evaluated the summary statistics to assess clinical value of the variants of interest. One of our genome-wide hits, rs382940, in the intron of *SLC44A1*, was associated with a faster rate of progression to reach HY3. *SLC44A1*, soluble carrier 44A1, is also referred to as choline transporter-like protein 1 (CTL1). The gene is ubiquitously expressed in the brain, colon, thyroid and other organs and is involved in choline transport. No associations with PD and this variant or the gene itself have been reported so far although it has been studied in several vitro and vivo studies.^{21–24} Further investigation is warranted. The search of the Brain eQTL database suggested that another GWAS-signal, rs61863020, was associated with *ADRA2A* expression, a gene reported to be associated with arousal/sleep state.²⁵ *ADRA2A* is consistently expressed in locus coeruleus as well as nigral dopamine neurons and pyramidal neurons of the human brain (<http://www.humanbraincode.org/>).²⁶ The *ADRA2A*-encoded alpha2 adrenoreceptor modulates norepinephrine levels. In addition, norepinephrine²⁷ and its receptors^{28,29} have been linked to PD in multiple model systems.

Interestingly, neither of the variants were reported to be associated with the incidence of Parkinson’s disease in the recent case-control analysis of PD.³ A case-control study cannot address some mechanisms which contribute to the heterogeneity of PD such as genetic effects only relevant to cases or interactions with PD treatments. The discrepancy between the case-control GWAS and our study may reflect this point.

In the targeted assessments, we confirmed the previous results of the associations between *GBA* risk variants and motor and cognitive aspects of PD.^{30–34} In contrast with *GBA* variants, association studies of *APOE* and cognitive function in PD have yielded mixed results [previously](#).^{35–39} Our data supported the association of *APOE* and cognitive function on two measurements; MMSE and MoCA.

The strength of the current study is the hypothesis-free approach of GWAS, which can be powerful in identifying new associations and expanding our biological knowledge-base. While the associations here should be replicated and further investigated with vivo/vitro experiments, these findings suggest the prioritization of the two variants and loci for future validations. We have reported all of the summary results on our publicly accessible site to

benefit researchers so that they may conduct/replicate the analysis of variants of interest in their own research.

The major limitation of this study is the heterogeneity of the cohorts, which is apparent in several ways: baseline characteristics, definitions of binomial outcomes, patterns for clinical care over the course of follow-up, the platforms for genotyping/sequencing, and sample acquisition/enrollment practices. By meta-analyzing at the dataset-level and exercising careful quality control throughout, we tried to extract the most generalizable and reliable results across cohorts.

Another limitation is the power of the study. Although we have aggregated the largest collection of longitudinal data in PD genetics so far, more data would be needed to identify relatively small differences expected within PD patients compared to the case-vs-control setting. From the meta-analysis results, we estimated that if we had 30% more participants in the same setting, we would have had at least one variant of the genome-wide significance ($5E-8$) in 21 out of 25 phenotypes (Supplemental Table 5). Additionally, our study results can be a valuable resource for validation and hypothesis testing as we have shown in our targeted analysis. The study website aims to provide other researchers with a tool to explore variants of their interest easily for all included phenotypes. (<https://pdgenetics.shinyapps.io/pdprogmetagwasbrowser/>)

In our survival analysis, we did not explicitly check the proportional hazard assumption. If a variant effect changed over time, the result would be interpreted as the average HR over time. Also, the result would be biased when one of the covariates violated the proportional hazard assumption in our model and it was also associated with the variant dosage. Replication is important in this regard as well.

Finally, the study participants were restricted to individuals with European ancestry. We are now striving to collect more data, including from populations that are under-represented in this study, to improve our understanding of this topic in future studies.

Conclusion

With 4,093 participants and 22,307 longitudinal data points over a median of 3.81 years, we performed 25 GWAS meta-analyses. We found two genome-wide significant signals: the rate to reach HY3 during the disease course and rs382940; and the prevalence of insomnia at baseline and rs61863020. We also conducted targeted assessments of previously published

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variants of interest using the GWAS results. These results provide valuable insights into how genetic factors contribute to the heterogeneity of PD and disease progression.

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Supplementary Materials

Appendix: The description of study cohorts [\(A\)](#). [IPDGC collaborators \(B\)](#)

Supplemental table 1: Cohort specific definitions of binomial outcomes

Supplemental table 2: Analytical models per datasets

Supplemental table 3: The study-specific genomic inflation factors

Supplemental table 4: The meta-analysis results of the association between risk variants and the clinical features and progression of Parkinson's disease

Supplemental table 5: The estimated study size to detect at least one variant with genome-wide significance

Supplemental figure 1: Gene-based test for reaching Hoehn and Yahr stage 3 or higher

Supplemental figure 2: Heatmap for the meta-analysis results of the association between risk variants and the clinical features and progression of Parkinson's disease

References

1. Postuma RB, Berg D, Stern M, et al. MDS clinical diagnostic criteria for Parkinson's disease. *Mov Disord*. 2015;30:1591–1601.
2. Keller MF, Saad M, Bras J, et al. Using genome-wide complex trait analysis to quantify “missing heritability” in Parkinson's disease. *Hum Mol Genet*. 2012;21:4996–5009.
3. Nalls MA, Blauwendraat C, Vallerga CL, et al. Expanding Parkinson's disease genetics: novel risk loci, genomic context, causal insights and heritable risk. *bioRxiv*. Epub 2019.
4. Leonard H, Blauwendraat C, Krohn L, et al. Genetic variability and potential effects on clinical trial outcomes: perspectives in Parkinson's disease. *bioRxiv* 2018.
5. Goetz CG, Poewe W, Rascol O, et al. Movement Disorder Society Task Force report on the Hoehn and Yahr staging scale: Status and recommendations The Movement Disorder Society Task Force on rating scales for Parkinson's disease. *Mov Disord*. 2004;19:1020–1028.
6. Goetz CG, Fahn S, Martinez-Martin P, et al. Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS): Process,

- format, and clinimetric testing plan. *Mov Disord*. 2007;22:41–47.
7. Nasreddine ZS, Phillips NA, Bédirian V, et al. The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. *J Am Geriatr Soc*. 2005;53:695–699.
 8. Nalls MA, Bras J, Hernandez DG, et al. NeuroX, a fast and efficient genotyping platform for investigation of neurodegenerative diseases. *Neurobiol Aging*. 2015;36:1605.e7-1605.e12.
 9. Purcell S, Neale B, Todd-Brown K, et al. PLINK: A Tool Set for Whole-Genome Association and Population-Based Linkage Analyses. *Am J Hum Genet*. 2007;81:559–575.
 10. Das S, Forer L, Schön herr S, et al. Next-generation genotype imputation service and methods. *Nat Genet*. 2016;48:1284–1287.
 11. Zhan X, Hu Y, Li B, Abecasis GR, Liu DJ. RVTESTS: an efficient and comprehensive tool for rare variant association analysis using sequence data: Table 1. *Bioinformatics*. 2016;32:1423–1426.
 12. Sä fken B, Rügamer D, Kneib T, Greven S. Conditional Model Selection in Mixed-Effects Models with cAIC4. Epub 2018 Mar 15.
 13. Willer CJ, Li Y, Abecasis GR. METAL: fast and efficient meta-analysis of genomewide association scans. *Bioinformatics*. 2010;26:2190–2191.
 14. Pruim RJ, Welch RP, Sanna S, et al. LocusZoom: regional visualization of genome-wide association scan results. *Bioinformatics*. 2010;26:2336–2337.
 15. Watanabe K, Taskesen E, van Bochoven A, Posthuma D. Functional mapping and annotation of genetic associations with FUMA. *Nat Commun*. 2017;8:1826.
 16. Vösa U, Claringbould P, Westra H-J, et al. Unraveling the polygenic architecture of complex traits using blood eQTL meta-analysis. *bioRxiv*. Epub 2018.
 17. Qi T, Wu Y, Zeng J, et al. Identifying gene targets for brain-related traits using transcriptomic and methylomic data from blood. *Nat Commun*. 2018;9:2282.
 18. Berge-Seidl V, Pihlström L, Maple-Grødem J, et al. The GBA variant E326K is associated with Parkinson's disease and explains a genome-wide association signal. *Neurosci Lett*. 2017;658:48–52.

19. Blauwendraat C, Bras JM, Nalls MA, Lewis PA, Hernandez DG, Singleton AB. Coding variation in GBA explains the majority of the SYT11-GBA Parkinson's disease GWAS locus. *Mov Disord*. 2018;33:1821–1823.
20. Iwaki H, Blauwendraat C, Leonard HL, et al. Genetic risk of Parkinson disease and progression: *Neurol Genet*. 2019;5:e348.
21. Machová E, O'Regan S, Newcombe J, et al. Detection of choline transporter-like 1 protein CTL1 in neuroblastoma × glioma cells and in the CNS, and its role in choline uptake. *J Neurochem*. Wiley Online Library; 2009;110:1297–1309.
22. Schenkel LC, Singh RK, Michel V, et al. Mechanism of choline deficiency and membrane alteration in postural orthostatic tachycardia syndrome primary skin fibroblasts. *FASEB J*. 2015;29:1663–1675.
23. Heffernan C, Jain MR, Liu T, et al. Nectin-like 4 Complexes with Choline Transporter-like Protein-1 and Regulates Schwann Cell Choline Homeostasis and Lipid Biogenesis in Vitro. *J Biol Chem*. 2017;292:4484–4498.
24. Gao P, He M, Zhang C, Geng C. Integrated analysis of gene expression signatures associated with colon cancer from three datasets. *Gene*. 2018;654:95–102.
25. Gelegen C, Gent TC, Ferretti V, et al. Staying awake - a genetic region that hinders α 2 adrenergic receptor agonist-induced sleep. *Eur J Neurosci*. 2014;40:2311–2319.
26. Dong X, Liao Z, Gritsch D, et al. Enhancers active in dopamine neurons are a primary link between genetic variation and neuropsychiatric disease. *Nat Neurosci*. 2018;21:1482–1492.
27. Tong J, Hornykiewicz O, Kish SJ. Inverse Relationship Between Brain Noradrenaline Level and Dopamine Loss in Parkinson Disease. *Arch Neurol*. 2006;63:1724.
28. Srinivasan J, Schmidt WJ. Treatment with α 2-adrenoceptor antagonist, 2-methoxy idazoxan, protects 6-hydroxydopamine-induced Parkinsonian symptoms in rats: neurochemical and behavioral evidence. *Behav Brain Res*. 2004;154:353–363.
29. Mittal S, Bjørnevik K, Im DS, et al. β 2-Adrenoreceptor is a regulator of the α -synuclein gene driving risk of Parkinson's disease. *Science (80-)*. 2017;357:891–898.
30. Winder-Rhodes SE, Evans JR, Ban M, et al. Glucocerebrosidase mutations influence the natural history of Parkinson's disease in a community-based incident cohort. *Brain*.

- 2013;136:392–399.
31. Brockmann K, Srulijes K, Pflederer S, et al. GBA -associated Parkinson's disease: Reduced survival and more rapid progression in a prospective longitudinal study. *Mov Disord*. 2015;30:407–411.
 32. Davis AA, Andruska KM, Benitez BA, Racette BA, Perlmutter JS, Cruchaga C. Variants in GBA , SNCA , and MAPT influence Parkinson disease risk, age at onset, and progression. *Neurobiol Aging*. 2016;37:209.e1-209.e7.
 33. Davis MY, Johnson CO, Leverenz JB, et al. Association of GBA Mutations and the E326K Polymorphism With Motor and Cognitive Progression in Parkinson Disease. *JAMA Neurol*. 2016;73:1217.
 34. Liu G, Boot B, Locascio JJ, et al. Specifically neuropathic Gaucher's mutations accelerate cognitive decline in Parkinson's. *Ann Neurol*. 2016;80:674–685.
 35. Huang X, Chen P, Kaufer DI, Tröster AI, Poole C. Apolipoprotein E and Dementia in Parkinson Disease. *Arch Neurol*. 2006;63:189.
 36. Kurz MW, Dekomien G, Nilsen OB, Larsen JP, Aarsland D, Alves G. APOE Alleles in Parkinson Disease and Their Relationship to Cognitive Decline: A Population-based, Longitudinal Study. *J Geriatr Psychiatry Neurol*. SAGE Publications Inc STM; 2009;22:166–170.
 37. Federoff M, Jimenez-Rolando B, Nalls MA, Singleton AB. A large study reveals no association between APOE and Parkinson's disease. *Neurobiol Dis*. 2012;46:389–392.
 38. Mata IF, Leverenz JB, Weintraub D, et al. APOE , MAPT , and SNCA Genes and Cognitive Performance in Parkinson Disease. *JAMA Neurol*. 2014;71:1405.
 39. Paul KC, Rausch R, Creek MM, et al. APOE, MAPT, and COMT and Parkinson's Disease Susceptibility and Cognitive Symptom Progression. *J Parkinsons Dis*. 2016;6:349–359.

Figure legends

Figure 1: Graphical overview of the analysis strategy.

* DIGPD cohort was analyzed separately depending on the genotyping system.

Rsq, R square; MAF, Minor allele frequency; HWE, Hardy–Weinberg equilibrium test; OR, Odds ratio; HR, Hazard ratio; PC, Principal components; AAD, Age at diagnosis; YfD, Years from diagnosis to observation; HY score, the score on the Hoehn and Yahr scale;

Figure 2: Locuszoom plots and forest plots of the two genome-wide significant hits. A: The locus plot for rs382940 which is associated with HY3. B: The locus plot for rs61863020 which is associated with insomnia. C: The forest plot for rs382940. D: The forest plot for rs61863020.

Figure 3: Heatmap of the Parkinson's disease GWAS loci associated with progression markers

Cream, P-value > 0.05; light green, P-value < 0.05; green: P-value < 0.002; blue, P-value < 5.68E-4; dark blue, P-value < 2.47E-5).

CONST, constipation; COGi, cognitive impairment; DEPR, depression; HY3, Hoehn and Yahr score; INS, insomnia; MMSE, Mini-Mental State Examination; MOCA, Montreal Cognitive Assessment; SEADL70, the modified Schwab and England Activities of Daily Living Scale; SLEEP, daytime sleepiness; UPDRS, Unified Parkinson's Disease Rating Scale (UPDRS) or the Movement Disorder Society revised UPDRS, scaled at the baseline (UPDRS1-3) or during the course.

Suffix of 'base' indicates the logistic regression model at baseline, 'surv' for the survival analysis over the course, and 'cont' for the linear mixed effect model for continuous outcome analyzed by linear mixed model.

Figure 4: Heatmap of the GBA and APOE variants associated with progression markers

Cream, P-value > 0.05; light green, P-value < 0.05; green: Bonferroni corrected P-value < 0.05;

CONST, constipation; COGi, cognitive impairment; DEPR, depression; HY3, Hoehn and Yahr score; INS, insomnia; MMSE, Mini-Mental State Examination; MOCA, Montreal Cognitive Assessment; SEADL, the modified Schwab and England Activities of Daily Living Scale; SLEEP, daytime sleepiness; UPDRS, Unified Parkinson's Disease Rating Scale (UPDRS) or the Movement Disorder Society revised UPDRS, scaled at the baseline (UPDRS1-3) or during the course.

Suffix of 'base' indicates the logistic regression model at baseline, 'surv' for the survival

analysis over the course, and ‘cont’ for the linear mixed effect model for continuous outcome analyzed by linear mixed model.

Author Roles

1. Research project: A. Conception, B. Organization, C. Execution; 2. Statistical Analysis: A. Design, B. Execution, C. Review and Critique; 3. Manuscript Preparation: A. Writing of the first draft, B. Review and Critique;

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Table 1. Summary characteristics of 13 datasets (12 cohorts)

	DATATO P	DIGPD_ chip	DIGPD_ neuroX	HBS	NET- PD_LS1	OSLO	PARKFI T	PARKWE ST	PDBP	PICNICS	PPMI	PRECEPT /POSTCEP T	PROPAR K
n	428	108	235	503	340	318	332	147	515	117	441	318	291
Total number of visits	3,303	268	811	1,206	2,209	2,086	664	294	2,360	358	2,436	4,983	1,599
Number of visits per participants (Median [1Q, 3Q])	7 [6,8] 1.22 (0.41)	2 [1, 3.25] 1.52 (1.60)	4 [3, 4.5] 2.54 (1.30)	3 [2,3] 1.53 (0.84)	7 [6, 8] 12.08 (6.91)	6 [3, 10] 1.97 (0.00)	2 [2,2] 3.04 (0.09)	2 [2,2] 1.97 (1.73)	5 [1, 7] 3.03 (1.62)	3 [2, 4] 4.88 (2.05)	6 [5, 7] 6.78 (0.95)	16 [14, 17] 4.64 (1.13)	6 [6, 6] 53.11 (10.58)
Follow up in years	58.73 (9.12)	59.04 (10.14)	60.44 (9.43)	62.27 (10.40)	60.84 (9.07)	54.43 (10.14)	60.85 (8.62)	67.16 (9.29)	58.59 (10.18)	68.95 (9.38)	61.05 (9.82)	59.45 (9.18)	53.11 (10.58)
Age at diagnosis	1.15 (1.16)	2.78 (1.56)	2.52 (1.57)	4.02 (4.62)	1.76 (4.69)	5.14 (4.40)	0.14 (0.12)	6.31 (5.44)	0.23 (0.48)	0.55 (0.54)	0.80 (0.84)	6.61 (4.67)	
Year from diagnosis	142 (33.2)	44 (40.7)	91 (38.7)	174 (34.6)	106 (33.3)	109 (32.8)	55 (37.4)	202 (39.2)	43 (36.8)	159 (36.1)	105 (33.0)	105 (36.1)	
Female (%)	197 (46.0)	68 (65.4)	151 (64.3)	420 (84.5)	-	22 (100.0)	314 (94.6)	85 (57.8)	426 (83.0)	62 (53.0)	242 (54.9)	198 (62.5)	271 (96.1)
Having HY2 or larger at baseline (%)	14.19 (3.29)	12.27 (2.92)	12.28 (3.17)	15.14 (1.72)	15.46 (2.23)	-	-	11.31 (3.24)	15.24 (4.56)	12.17 (2.89)	15.58 (2.98)	15.93 (3.15)	11.95 (4.10)
Years of education	161 (3.29)	163 (2.92)	353 (3.17)	171 (50.6)	-	-	-	409 (83.1)	35 (29.9)	199 (3.0)	199 (0.0)	199 (0.0)	199 (68.4)
Use of levodopa (%)	0 (0.0)	64 (59.8)	66 (28.4)	198 (39.4)	231 (68.3)	-	-	277 (56.3)	22 (18.8)	218 (0.0)	218 (0.0)	218 (0.3)	218 (74.9)
Use of agonist (%)	0 (0.0)	88 (81.5)	66 (28.4)	-	-	-	-	295 (63.6)	185 (44.6)	170 (63.7)	170 (63.7)	170 (63.7)	
Hyposmia (%)	0 (0.0)	33 (30.8)	2 (0.9)	59 (11.9)	27 (7.9)	-	(16.6)	119 (23.2)	11 (9.4)	35 (7.9)	3 (0.9)	76 (27.1)	
Cognitive impairment (%)	24 (5.6)	1 (0.9)	2 (0.9)	198 (39.9)	87 (25.7)	-	-	176 (37.3)	0 (0.0)	0 (0.0)	-	92 (32.3)	
Motor fluctuations (%)	-	14 (13.1)	13 (5.5)	168 (33.8)	5 (1.5)	-	-	118 (25.0)	0 (0.0)	0 (0.0)	-	80 (27.8)	
Dyskinesias (%)	3 (0.7)	4 (3.7)	77 (33.3)	28 (10.3)	31 (9.2)	-	-	26 (22.2)	141 (33.8)	72 (22.6)	48 (16.6)		
Depression (%)	11 (2.6)	29 (27.1)	34 (14.5)	30 (10.4)	-	-	-	107 (24.4)	-	(0.65)	-	-	-
Restless legs syndrome (%)	-	16 (15.7)	48 (20.7)	-	-	-	-	255 (54.0)	27 (23.1)	149 (33.8)	-	137 (47.1)	
Constipation (%)	9 (2.1)	17 (16.0)	-	-	-	-	-	217 (49.4)	-	(24.9)	-	-	-
REM sleep behavior disorder (%)	-	-	-	-	-	-	-	178 (37.7)	24 (20.5)	61 (14.7)	-	125 (43.0)	
Daytime sleepiness (%)	3 (0.7)	51 (48.6)	104 (44.3)	-	-	-	-	23 (15.6)					

1	Insomnia (%)	11 (2.6)	31 (30.4)	86 (36.6)	170 (33.9)	-	-	-	45 (30.6)	332 (70.3)	59 (50.4)	109 (24.7)	-	83 (28.5)
2	Hoehn Yahr scale 3 or greater							17			12			115
3	(%)	0 (0.0)	2 (1.9)	3 (1.3)	59 (11.9)	10 (2.9)	0 (0.0)	(5.1)	11 (7.5)	81 (15.8)	(10.3)	2 (0.5)	0 (0.0)	(40.8)
4	SEADL 70 or less (%)	3 (0.7)	30 (30.0)	12 (5.1)	-	2 (0.6)	-	-	5 (3.4)	75 (15.9)	-	2 (0.5)	1 (0.3)	-
5		1.61	1.76	1.77	2.13		3.27	2.08	1.87	2.03	1.63	1.50	1.75	2.51
6	Hoehn Yahr scale	(0.53)	(0.56)	(0.54)	(0.63)	-	(0.55)	(0.33)	(0.58)	(0.73)	(0.66)	(0.50)	(0.48)	(0.79)
7		-0.07	0.08	-0.03	-0.00		-0.06	-0.02	-0.02	-0.07	-0.01		0.02	
8	UPDRS_scaled	(0.98)	(1.00)	(0.96)	(1.00)	0.00 (1.01)	-	(0.96)	(1.01)	(1.01)	(0.98)	-	(1.00)	-
9			-0.10	-0.02	0.01				-0.03	0.03		0.00	-0.03	
10	UPDRS1_scaled	-	(0.99)	(0.90)	(1.01)	0.01 (1.06)	-	-	(1.00)	(1.01)	-	(4.31)	(0.96)	-
11			0.13	-0.06	0.00				-0.03	-0.00		0.00	-0.01	
12	UPDRS2_scaled	-	(1.01)	(0.98)	(1.00)	0.01 (0.98)	-	-	(1.00)	(1.01)	-	(4.19)	(1.00)	-
13			0.09	-0.02	-0.01		0.61		-0.01	-0.09		-0.00	0.04	
14	UPDRS3_scaled	-	(0.99)	(0.96)	(1.00)	0.00 (1.00)	(1.21)	-	(1.00)	(1.00)	-	(8.87)	(0.99)	-
15			-0.09	-0.17	-0.20				-0.25	-0.12				
16	UPDRS4_scaled	-	(1.55)	(0.81)	(0.86)	-0.33 (0.71)	-	-	(0.86)	(0.94)	-	-	-	-
17		29.01	28.59	28.21	28.39			28.09	27.86		28.70		29.28	27.05
18	MMSE	(1.32)	(1.66)	(1.75)	(2.17)	-	-	(1.61)	(2.29)	-	(1.44)	-	(1.08)	(2.50)
19		91.56	64.96	88.54		91.88			89.39	84.58		93.79	92.78	
20	SEADL	(6.49)	(41.02)	(14.94)	-	(5.84)	-	-	(7.42)	(14.84)	-	(6.11)	(5.26)	-

Continous variables were summarized in Mean (SD). MMSE, Mini Mental State Exam-ition; Montreal Cognitive Assessment, SEADL, Schwab and England Activities of Daily Living Scale; UPDRS, Unified Parkinson Disease Rating Scale; MDS-UPDRS, Movment Disorder Society revised version of UPDRS.

Figure 1. Graphical overview of the analysis strategy.

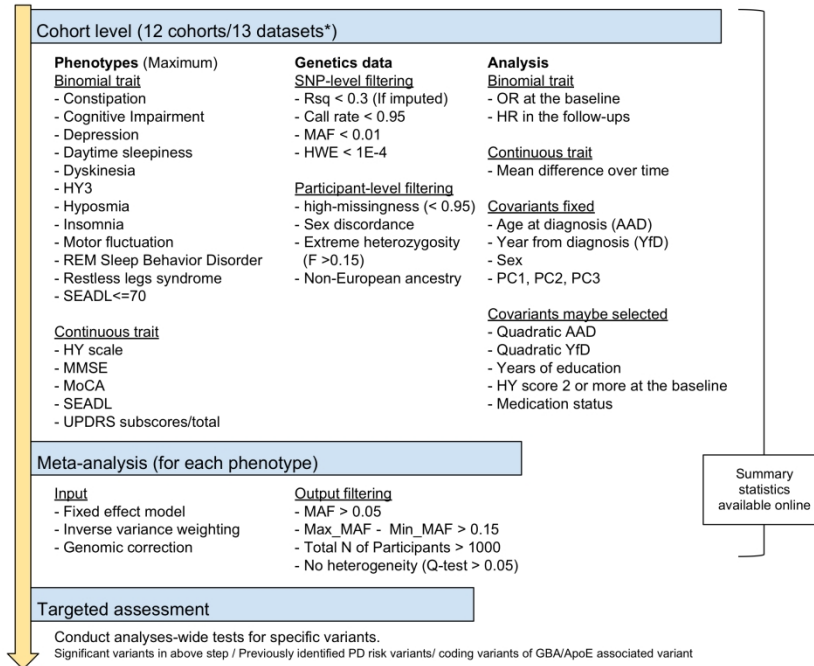


Figure1

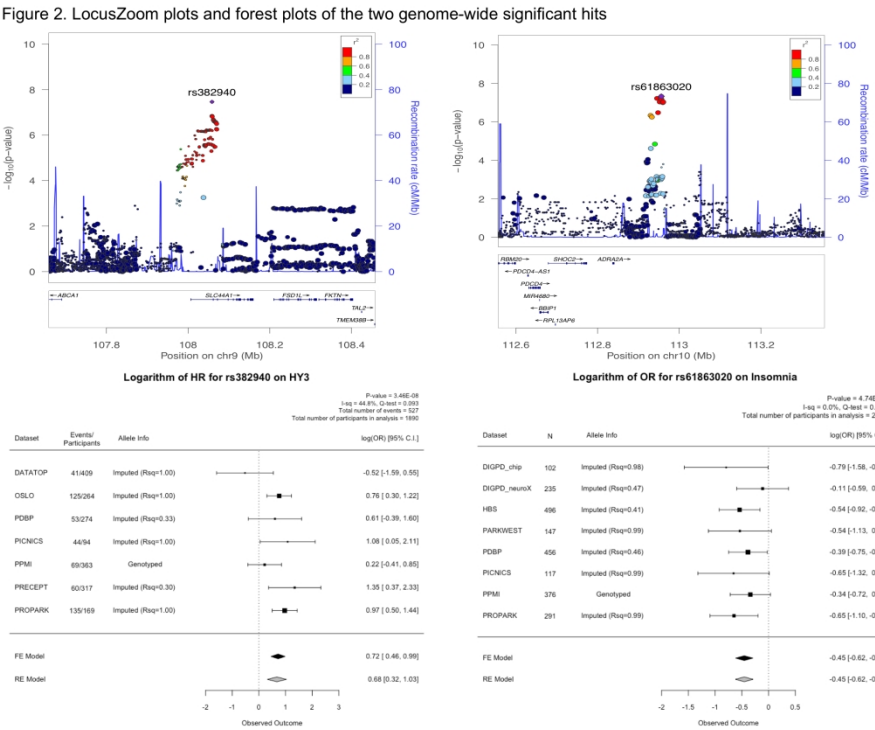


Figure2

Figure 3. Heatmap of the Parkinson's disease GWAS loci associated with progression markers.

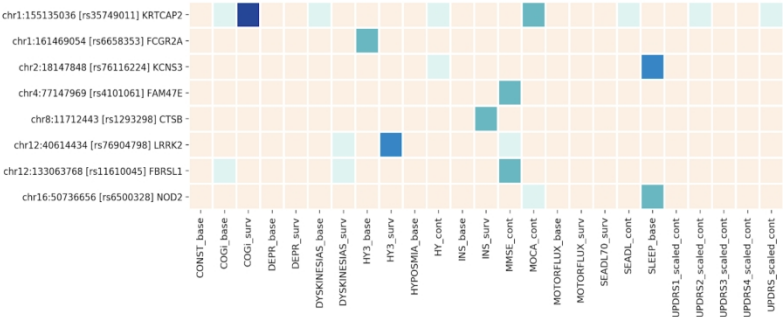


Figure3

Figure 4. Heatmap of the GBA and APOE variants associated with progression markers

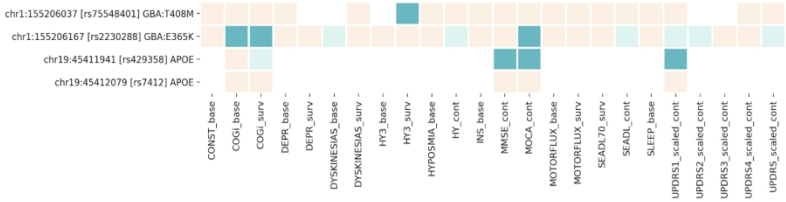
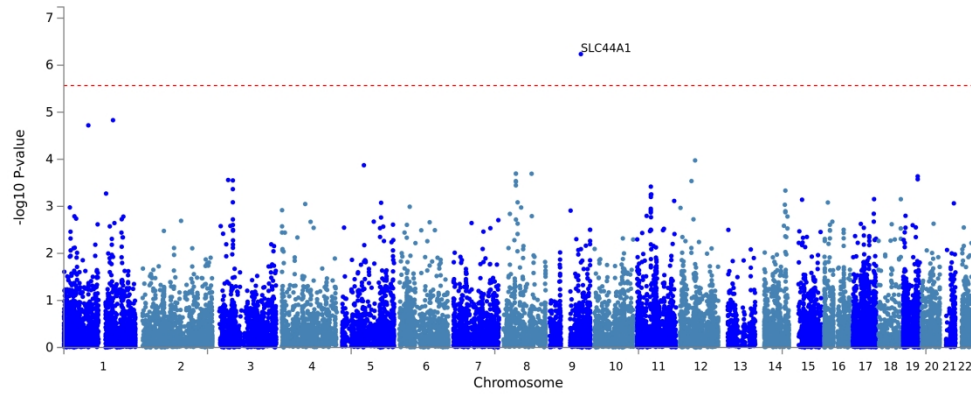


Figure3



248x107mm (300 x 300 DPI)



Supplementary Table 1. Cohort specific definitions of binomial outcomes

	DATATOP	DIGPD	HBS	NET-PD LS1	Oslo	ParkFit	ParkWest	PDBP	PICNICS	PPMI	εCEPT/ PostCEF	ProPark
hyposmia	-	NMS question-ir	-	-	-	-	"Is your sense of	UPSIT<21	-	UPSIT<21	UPSIT<21	study question
cognitive impairment	MMSE<27	DSM IV criteria	MMSE<27	SCOPA_COG<2	-	MMSE<27	MMSE<27	MoCA<24	MDS dementia cr MoCA<24	MMSE<27	-	SCOPA-COG value <23
motor fluctuations	-	Neurologist diagn	UPDRS4 Q32-Q	UPDRS4 off tim	-	-	UPDRS Q35 0/	MDS-UPDRS4	MDS-UPDRS 4.	MDS-UPDRS 4.	-	SPES/SCOPA item 20 >0
dyskinesia	Report of dyskine	Neurologist diagn	UPDRS4 Q36-Q	UPDRS4 dyskine	-	-	UPDRS Q32 >/	MDS-UPDRS4	MDS-UPDRS 4.	MDS-UPDRS 4.	-	SPES/SCOPA item 18 >0
depression	Report of depress	Neurologist diagn	GDS15 >5	BDI>14	-	-	UPDRS 3 >= 2	HDRS>9	Beck depression i	GDS15 >5	UPDRS item 3 >1	Beck DI score >14
restless legs syndrome	-	RLS criteria	Past medical histo	-	-	-	-	MSQ3 yes	-	RBDSQ, RLS ye	-	-
constipation	Report of constip	NMS question-ir	-	-	-	-	-	MDS-UPDRS1	MDS UPDRS ite	MDS-UPDRS1	MDS-UPDRS1	SCOPA-AUT item 5 >0
RBD	-	-	-	-	-	-	-	MSQ1 yes	-	RBDSQ>5	-	-
daytime sleepiess	Report of drowsii	Neurologist diagn	-	-	-	-	Epworth > 9	EPworth > 9	ESS>=10 OR M	EPworth > 9	MDS-UPDRS1	SCOPA-SLEEP daytime sleepiness (section D) >4
insomnia	Report of insomn	Neurologist diagn	UPDRS4 Q41	-	-	-	"Do you have pre	UPDRS.Ins>0	MDS-UPDRS ite	MDS-UPDRS	Ir MDS-UPDRS	SCOPA-SLEEP Nighttime (section B) S >6

BDI, Beck's Depression Inventory; GDS, Geriatric Depression Scale; HDRS, Hamilton Depression Rating Scale; MMSE, the Mini-Mental State Examination; MoCA Montreal Cognitive Assessment; MSQ, Mayo Sleep Questionnaire; NMS, Non-motor Symptoms Questionnaire; RBD, REM sleep Behavior Disorder

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Supplemental Table 2. Analytical models per datasets			
DATASET	ANALYSIS	OUTCOME	MODEL
DATATOP	base	COGi	AAD+BLDfDIAG+FEMALE+YEARSEduc
DATATOP	cont	HY	AAD+FEMALE+YEARfDIAG
DATATOP	cont	MMSE	AAD+FEMALE+YEARSEduc+YEARfDIAG+ YEARfDIAGsq
DATATOP	cont	SEADL	AAD+FEMALE+YEARfDIAG+YEARfDIAGsq
DATATOP	cont	UPDRS_scaled	AAD+FEMALE+YEARSEduc+YEARfDIAG+ YEARfDIAGsq
DATATOP	surv	COGi	AAD+AADsq+BLDfDIAG+BLDfDIAGsq+FEMALE+YEARSEduc
DATATOP	surv	HY3	AAD+BLDfDIAG+BLDfDIAGsq+FEMALE+firstHY2
DATATOP	surv	SEADL70	AAD+BLDfDIAG+FEMALE+YEARSEduc+firstHY2
DIGPD_chip	base	DEPR	AAD+BLDfDIAG+BLDfDIAGsq+LEVODOPA+FEMALE+YEARSEduc
DIGPD_chip	base	HYPOSMIA	AAD+BLDfDIAG+FEMALE+YEARSEduc
DIGPD_chip	base	INS	AAD+BLDfDIAG+FEMALE
DIGPD_chip	base	SEADL70	AAD+AADsq+BLDfDIAG+BLDfDIAGsq+FEMALE+YEARSEduc
DIGPD_chip	base	SLEEP	AAD+BLDfDIAG+DRT+FEMALE
DIGPD_chip	cont	HY	AAD+FEMALE+YEARSEduc+YEARfDIAG+firstHY2
DIGPD_chip	cont	MMSE	AAD+FEMALE+YEARSEduc+YEARfDIAG+firstHY2
DIGPD_chip	cont	SEADL	AAD+AADsq+AGONIST+LEVODOPA+FEMALE+YEARSEduc+YEARfDIAG
DIGPD_chip	cont	UPDRS_scaled	AAD+AADsq+LEVODOPA+FEMALE+YEARSEduc+YEARfDIAG+firstHY2
DIGPD_chip	cont	UPDRS1_scaled	AAD+AADsq+FEMALE+YEARfDIAG
DIGPD_chip	cont	UPDRS2_scaled	AAD+AADsq+LEVODOPA+FEMALE+YEARfDIAG+firstHY2
DIGPD_chip	cont	UPDRS3_scaled	AAD+AADsq+LEVODOPA+FEMALE+YEARSEduc+YEARfDIAG
DIGPD_chip	cont	UPDRS4_scaled	AAD+FEMALE+YEARfDIAG
DIGPD_neuroX	base	CONST	AAD+AGONIST+BLDfDIAG+BLDfDIAGsq+FEMALE
DIGPD_neuroX	base	DEPR	AAD+BLDfDIAG+FEMALE
DIGPD_neuroX	base	HYPOSMIA	AAD+BLDfDIAG+FEMALE+YEARSEduc
DIGPD_neuroX	base	INS	AAD+BLDfDIAG+FEMALE
DIGPD_neuroX	base	MOTORFLUX	AAD+BLDfDIAG+BLDfDIAGsq+LEVODOPA+DRT+FEMALE
DIGPD_neuroX	base	RL	AAD+BLDfDIAG+FEMALE
DIGPD_neuroX	base	SLEEP	AAD+BLDfDIAG+BLDfDIAGsq+FEMALE+firstHY2
DIGPD_neuroX	cont	HY	AAD+AGONIST+DRT+FEMALE+YEARSEduc+YEARfDIAG+YEARfDIAGsq+firstHY2
DIGPD_neuroX	cont	MMSE	AAD+AGONIST+LEVODOPA+FEMALE+YEARSEduc+YEARfDIAG+YEARfDIAGsq+firstHY2
DIGPD_neuroX	cont	SEADL	AAD+AGONIST+FEMALE+YEARfDIAG+YEARfDIAGsq
DIGPD_neuroX	cont	UPDRS_scaled	AAD+AADsq+LEVODOPA+FEMALE+YEARSEduc+YEARfDIAG+YEARfDIAGsq+firstHY2
DIGPD_neuroX	cont	UPDRS1_scaled	AAD+FEMALE+YEARfDIAG+YEARfDIAGsq+firstHY2
DIGPD_neuroX	cont	UPDRS2_scaled	AAD+AADsq+FEMALE+YEARSEduc+YEARfDIAG+YEARfDIAGsq+firstHY2
DIGPD_neuroX	cont	UPDRS3_scaled	AAD+AADsq+AGONIST+LEVODOPA+DRT+FEMALE+YEARfDIAG+YEARfDIAGsq
DIGPD_neuroX	cont	UPDRS4_scaled	AAD+AADsq+FEMALE+YEARfDIAG+YEARfDIAGsq
DIGPD_neuroX	surv	CONST	AAD+AADsq+BLDfDIAG+LEVODOPA+FEMALE+YEARSEduc+firstHY2
DIGPD_neuroX	surv	DEPR	AAD+BLDfDIAG+FEMALE
DIGPD_neuroX	surv	DYSKINESIAS	AAD+BLDfDIAG+LEVODOPA+FEMALE
DIGPD_neuroX	surv	HYPOSMIA	AAD+BLDfDIAG+LEVODOPA+FEMALE+firstHY2
DIGPD_neuroX	surv	INS	AAD+AGONIST+BLDfDIAG+BLDfDIAGsq+FEMALE+YEARSEduc
DIGPD_neuroX	surv	MOTORFLUX	AAD+BLDfDIAG+LEVODOPA+FEMALE+firstHY2
DIGPD_neuroX	surv	RL	AAD+AGONIST+BLDfDIAG+FEMALE
DIGPD_neuroX	surv	SLEEP	AAD+AGONIST+BLDfDIAG+FEMALE+YEARSEduc
HBS	base	COGi	AAD+AGONIST+BLDfDIAG+LEVODOPA+FEMALE+YEARSEduc
HBS	base	DEPR	AAD+AGONIST+BLDfDIAG+LEVODOPA+FEMALE+firstHY2
HBS	base	DYSKINESIAS	AAD+BLDfDIAG+LEVODOPA+FEMALE+YEARSEduc+firstHY2
HBS	base	HY3	AAD+AGONIST+BLDfDIAG+LEVODOPA+FEMALE+YEARSEduc+firstHY2
HBS	base	INS	AAD+BLDfDIAG+LEVODOPA+FEMALE+firstHY2
HBS	base	MOTORFLUX	AAD+BLDfDIAG+BLDfDIAGsq+LEVODOPA+FEMALE+firstHY2
HBS	base	RL	AAD+AADsq+AGONIST+BLDfDIAG+FEMALE+YEARSEduc+firstHY2
HBS	cont	HY	AAD+LEVODOPA+FEMALE+YEARfDIAG+YEARfDIAGsq+firstHY2
HBS	cont	MMSE	AAD+AADsq+AGONIST+FEMALE+YEARSEduc+YEARfDIAG
HBS	cont	UPDRS_scaled	AAD+AGONIST+LEVODOPA+FEMALE+YEARfDIAG+YEARfDIAGsq
HBS	cont	UPDRS1_scaled	AAD+FEMALE+YEARfDIAG+firstHY2
HBS	cont	UPDRS2_scaled	AAD+LEVODOPA+DRT+FEMALE+YEARfDIAG+YEARfDIAGsq+firstHY2
HBS	cont	UPDRS3_scaled	AAD+AGONIST+LEVODOPA+FEMALE+YEARfDIAG+YEARfDIAGsq
HBS	cont	UPDRS4_scaled	AAD+LEVODOPA+FEMALE+YEARfDIAG+YEARfDIAGsq+firstHY2
HBS	surv	COGi	AAD+BLDfDIAG+FEMALE+YEARSEduc
HBS	surv	DEPR	AAD+BLDfDIAG+BLDfDIAGsq+LEVODOPA+FEMALE
HBS	surv	DYSKINESIAS	AAD+BLDfDIAG+BLDfDIAGsq+LEVODOPA+FEMALE
HBS	surv	HY3	AAD+BLDfDIAG+DRT+FEMALE+firstHY2
HBS	surv	INS	AAD+BLDfDIAG+FEMALE+firstHY2
HBS	surv	MOTORFLUX	AAD+BLDfDIAG+DRT+FEMALE
NET-PD_Ls1	base	COGi	AAD+BLDfDIAG+LEVODOPA+FEMALE+YEARSEduc
NET-PD_Ls1	base	DEPR	AAD+BLDfDIAG+FEMALE+YEARSEduc
NET-PD_Ls1	base	MOTORFLUX	AAD+BLDfDIAG+LEVODOPA+FEMALE
NET-PD_Ls1	cont	SEADL	AAD+AADsq+LEVODOPA+FEMALE+YEARSEduc+YEARfDIAG+YEARfDIAGsq
NET-PD_Ls1	cont	UPDRS_scaled	AAD+AADsq+LEVODOPA+DRT+FEMALE+YEARSEduc+YEARfDIAG+YEARfDIAGsq
NET-PD_Ls1	cont	UPDRS1_scaled	AAD+AADsq+FEMALE+YEARSEduc+YEARfDIAG+YEARfDIAGsq
NET-PD_Ls1	cont	UPDRS2_scaled	AAD+AADsq+LEVODOPA+DRT+FEMALE+YEARSEduc+YEARfDIAG+YEARfDIAGsq
NET-PD_Ls1	cont	UPDRS3_scaled	AAD+AADsq+LEVODOPA+DRT+FEMALE+YEARSEduc+YEARfDIAG
NET-PD_Ls1	cont	UPDRS4_scaled	AAD+FEMALE+YEARfDIAG+YEARfDIAGsq
NET-PD_Ls1	surv	COGi	AAD+BLDfDIAG+FEMALE
NET-PD_Ls1	surv	DEPR	AAD+BLDfDIAG+BLDfDIAGsq+FEMALE+YEARSEduc
NET-PD_Ls1	surv	DYSKINESIAS	AAD+AADsq+BLDfDIAG+LEVODOPA+FEMALE
NET-PD_Ls1	surv	HY3	AAD+BLDfDIAG+FEMALE
NET-PD_Ls1	surv	MOTORFLUX	AAD+BLDfDIAG+LEVODOPA+FEMALE
NET-PD_Ls1	surv	SEADL70	AAD+AADsq+BLDfDIAG+LEVODOPA+FEMALE
OSLO	cont	HY	AAD+FEMALE+YEARfDIAG+YEARfDIAGsq
OSLO	cont	UPDRS3_scaled	AAD+AADsq+FEMALE+YEARfDIAG+YEARfDIAGsq
OSLO	surv	HY3	AAD+AADsq+FEMALE
PARKFIT	base	COGi	AAD+BLDfDIAG+FEMALE
PARKFIT	cont	HY	AAD+AADsq+FEMALE+YEARfDIAG+YEARfDIAGsq+firstHY2
PARKFIT	cont	UPDRS_scaled	AAD+AADsq+FEMALE+YEARfDIAG+YEARfDIAGsq+firstHY2
PARKFIT	sngl	MMSE	AAD+FEMALE+YEARfDIAG
PARKWEST	base	COGi	AAD+AADsq+BLDfDIAG+FEMALE+YEARSEduc
PARKWEST	base	HYPOSMIA	AAD+BLDfDIAG+FEMALE+firstHY2
PARKWEST	base	INS	AAD+BLDfDIAG+FEMALE
PARKWEST	base	SLEEP	AAD+BLDfDIAG+FEMALE
PARKWEST	cont	HY	AAD+AADsq+AGONIST+LEVODOPA+FEMALE+YEARSEduc+YEARfDIAG+firstHY2
PARKWEST	cont	MMSE	AAD+AGONIST+FEMALE+YEARSEduc+YEARfDIAG+YEARfDIAGsq
PARKWEST	cont	SEADL	AAD+AADsq+LEVODOPA+FEMALE+YEARSEduc+YEARfDIAG+firstHY2
PARKWEST	cont	UPDRS_scaled	AAD+AGONIST+LEVODOPA+FEMALE+YEARSEduc+YEARfDIAG+firstHY2
PARKWEST	cont	UPDRS1_scaled	AAD+LEVODOPA+FEMALE+YEARSEduc+YEARfDIAG+firstHY2
PARKWEST	cont	UPDRS2_scaled	AAD+AADsq+LEVODOPA+FEMALE+YEARSEduc+YEARfDIAG+firstHY2
PARKWEST	cont	UPDRS3_scaled	AAD+AGONIST+LEVODOPA+FEMALE+YEARSEduc+YEARfDIAG+YEARfDIAGsq
PARKWEST	cont	UPDRS4_scaled	AAD+AGONIST+DRT+FEMALE+YEARfDIAG+firstHY2

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2	PARKWEST	surv	COGi	AAD+BLDfDIAG+FEMALE+firstHY2	
3	PDBP	base	CONST	AAD+BLDfDIAG+BLDfDIAGsq+LEVODOPA+FEMALE+YEARS EDUC	
4	PDBP	base	COGi	AAD+BLDfDIAG+DRT+FEMALE+YEARS EDUC	
5	PDBP	base	DEPR	AAD+BLDfDIAG+FEMALE	
6	PDBP	base	DYSKINESIAS	AAD+AADsq+BLDfDIAG+BLDfDIAGsq+LEVODOPA+DRT+FEMALE+YEARS EDUC	
7	PDBP	base	HY3	AAD+AADsq+BLDfDIAG+FEMALE+firstHY2	
8	PDBP	base	HYPOSMIA	AAD+BLDfDIAG+FEMALE	
9	PDBP	base	INS	AAD+AADsq+AGONIST+BLDfDIAG+LEVODOPA+FEMALE+YEARS EDUC	
10	PDBP	base	MOTORFLUX	AAD+BLDfDIAG+LEVODOPA+FEMALE+firstHY2	
11	PDBP	base	RBD	AAD+AADsq+BLDfDIAG+FEMALE+firstHY2+YEARS EDUC	
12	PDBP	base	RL	AAD+BLDfDIAG+LEVODOPA+FEMALE	
13	PDBP	base	SEADL70	AAD+AADsq+BLDfDIAG+BLDfDIAGsq+LEVODOPA+DRT+FEMALE+firstHY2	
14	PDBP	base	SLEEP	AAD+AADsq+AGONIST+BLDfDIAG+BLDfDIAGsq+FEMALE	
15	PDBP	cont	HY	AAD+LEVODOPA+FEMALE+firstHY2+YEARfDIAG	
16	PDBP	cont	MOCA	AAD+FEMALE+YEARfDIAG+YEARS EDUC	
17	PDBP	cont	SEADL	AAD+AADsq+AGONIST+DRT+FEMALE+firstHY2+YEARfDIAG+YEARS EDUC	
18	PDBP	cont	UPDRS_scaled	AAD+AADsq+AGONIST+DRT+FEMALE+firstHY2+YEARfDIAG+YEARfDIAGsq+YEARS EDUC	
19	PDBP	cont	UPDRS1_scaled	AAD+AGONIST+FEMALE+firstHY2+YEARfDIAG+YEARfDIAGsq+YEARS EDUC	
20	PDBP	cont	UPDRS2_scaled	AAD+AADsq+LEVODOPA+FEMALE+firstHY2+YEARfDIAG+YEARfDIAGsq+YEARS EDUC	
21	PDBP	cont	UPDRS3_scaled	AAD+AGONIST+DRT+FEMALE+YEARfDIAG+YEARfDIAGsq+YEARS EDUC	
22	PDBP	cont	UPDRS4_scaled	AAD+AADsq+FEMALE+firstHY2+YEARfDIAG+YEARfDIAGsq	
23	PDBP	surv	CONST	AAD+AADsq+AGONIST+BLDfDIAG+LEVODOPA+FEMALE	
24	PDBP	surv	COGi	AAD+BLDfDIAG+FEMALE+YEARS EDUC	
25	PDBP	surv	DEPR	AAD+AADsq+BLDfDIAG+BLDfDIAGsq+FEMALE+YEARS EDUC	
26	PDBP	surv	DYSKINESIAS	AAD+AADsq+BLDfDIAG+DRT+FEMALE+firstHY2+YEARS EDUC	
27	PDBP	surv	HY3	AAD+BLDfDIAG+FEMALE	
28	PDBP	surv	HYPOSMIA	AAD+BLDfDIAG+FEMALE+firstHY2	
29	PDBP	surv	INS	AAD+BLDfDIAG+FEMALE	
30	PDBP	surv	MOTORFLUX	AAD+BLDfDIAG+LEVODOPA+DRT+FEMALE+firstHY2	
31	PDBP	surv	RBD	AAD+BLDfDIAG+LEVODOPA+FEMALE	
32	PDBP	surv	RL	AAD+AGONIST+BLDfDIAG+LEVODOPA+FEMALE+YEARS EDUC	
33	PDBP	surv	SEADL70	AAD+BLDfDIAG+FEMALE+firstHY2	
34	PDBP	surv	SLEEP	AAD+AGONIST+BLDfDIAG+DRT+FEMALE+YEARS EDUC	
35	PICNICS	base	CONST	AAD+BLDfDIAG+LEVODOPA+FEMALE	
36	PICNICS	base	DEPR	AAD+AGONIST+BLDfDIAG+FEMALE	
37	PICNICS	base	INS	AAD+BLDfDIAG+LEVODOPA+FEMALE+YEARS EDUC	
38	PICNICS	base	SLEEP	AAD+BLDfDIAG+LEVODOPA+DRT+FEMALE	
39	PICNICS	cont	HY	AAD+FEMALE+YEARfDIAG+YEARfDIAGsq+firstHY2	
40	PICNICS	cont	MMSE	AAD+AADsq+LEVODOPA+FEMALE+YEARS EDUC+YEARfDIAG+firstHY2	
41	PICNICS	cont	MOCA	AAD+FEMALE+YEARS EDUC+YEARfDIAG+YEARfDIAGsq+firstHY2	
42	PICNICS	cont	UPDRS_scaled	AAD+FEMALE+YEARS EDUC+YEARfDIAG+YEARfDIAGsq+firstHY2	
43	PICNICS	surv	CONST	AAD+BLDfDIAG+FEMALE	
44	PICNICS	surv	COGi	AAD+BLDfDIAG+BLDfDIAGsq+DRT+FEMALE	
45	PICNICS	surv	DEPR	AAD+AADsq+BLDfDIAG+LEVODOPA+FEMALE+YEARS EDUC	
46	PICNICS	surv	HY3	AAD+BLDfDIAG+BLDfDIAGsq+DRT+FEMALE+firstHY2	
47	PICNICS	surv	INS	AAD+BLDfDIAG+FEMALE+YEARS EDUC	
48	PICNICS	surv	MOTORFLUX	AAD+AGONIST+BLDfDIAG+BLDfDIAGsq+FEMALE+firstHY2	
49	PICNICS	surv	SLEEP	AAD+AGONIST+BLDfDIAG+FEMALE	
50	PPMI	base	CONST	AAD+AADsq+BLDfDIAG+FEMALE	
51	PPMI	base	COGi	AAD+AADsq+BLDfDIAG+FEMALE+YEARS EDUC	
52	PPMI	base	HYPOSMIA	AAD+AADsq+BLDfDIAG+FEMALE	
53	PPMI	base	INS	AAD+BLDfDIAG+FEMALE	
54	PPMI	base	RBD	AAD+AADsq+BLDfDIAG+FEMALE	
55	PPMI	base	SLEEP	AAD+BLDfDIAG+FEMALE+YEARS EDUC	
56	PPMI	cont	HY	AAD+AADsq+FEMALE+MED+YEARfDIAG+YEARfDIAGsq	
57	PPMI	cont	MOCA	AAD+DRT+FEMALE+YEARS EDUC+YEARfDIAG	
58	PPMI	cont	SEADL	AAD+DRT+FEMALE+LEVODOPA+YEARS EDUC+YEARfDIAG+YEARfDIAGsq	
59	PPMI	cont	UPDRS1	AAD+AGONIST+FEMALE+YEARfDIAG	
60	PPMI	cont	UPDRS2	AAD+DRT+FEMALE+LEVODOPA+YEARfDIAG+YEARfDIAGsq	
	PPMI	cont	UPDRS3	AAD+FEMALE+MED+YEARfDIAG+YEARfDIAGsq	
	PPMI	surv	CONST	AAD+BLDfDIAG+FEMALE	
	PPMI	surv	COGi	AAD+BLDfDIAG+FEMALE+firstHY2	
	PPMI	surv	DYSKINESIAS	AAD+BLDfDIAG+FEMALE+YEARS EDUC	
	PPMI	surv	HY3	AAD+BLDfDIAG+FEMALE+firstHY2	
	PPMI	surv	INS	AAD+BLDfDIAG+FEMALE	
	PPMI	surv	MOTORFLUX	AAD+AADsq+BLDfDIAG+FEMALE+YEARS EDUC	
	PPMI	surv	RBD	AAD+BLDfDIAG+FEMALE+YEARS EDUC+firstHY2	
	PPMI	surv	SEADL70	AAD+AADsq+BLDfDIAG+BLDfDIAGsq+FEMALE	
	PPMI	surv	SLEEP	AAD+BLDfDIAG+BLDfDIAGsq+FEMALE	
	PRECEPT	base	DEPR	AAD+BLDfDIAG+FEMALE+firstHY2	
	PRECEPT	cont	HY	AAD+AADsq+AGONIST+FEMALE+YEARS EDUC+YEARfDIAG+YEARfDIAGsq+firstHY2	
	PRECEPT	cont	MMSE	AAD+AADsq+AGONIST+FEMALE+YEARS EDUC+YEARfDIAG	
	PRECEPT	cont	MOCA	AAD+AADsq+FEMALE+YEARS EDUC+YEARfDIAG+YEARfDIAGsq+firstHY2	
	PRECEPT	cont	SEADL	AAD+AADsq+AGONIST+LEVODOPA+DRT+FEMALE+YEARS EDUC+YEARfDIAG+YEARfDIAGsq+firstHY2	
	PRECEPT	cont	UPDRS_scaled	AAD+AADsq+AGONIST+DRT+FEMALE+YEARS EDUC+YEARfDIAG+YEARfDIAGsq+firstHY2	
	PRECEPT	cont	UPDRS1_scaled	AAD+AGONIST+DRT+FEMALE+YEARS EDUC+YEARfDIAG+firstHY2	
	PRECEPT	cont	UPDRS2_scaled	AAD+AADsq+AGONIST+LEVODOPA+DRT+FEMALE+YEARS EDUC+YEARfDIAG+YEARfDIAGsq+firstHY2	
	PRECEPT	cont	UPDRS3_scaled	AAD+AADsq+AGONIST+LEVODOPA+DRT+FEMALE+YEARS EDUC+YEARfDIAG+YEARfDIAGsq	
	PRECEPT	surv	CONST	AAD+BLDfDIAG+FEMALE	
	PRECEPT	surv	COGi	AAD+BLDfDIAG+FEMALE+YEARS EDUC	
	PRECEPT	surv	DEPR	AAD+BLDfDIAG+FEMALE+YEARS EDUC	
	PRECEPT	surv	DYSKINESIAS	AAD+AGONIST+BLDfDIAG+LEVODOPA+FEMALE+firstHY2	
	PRECEPT	surv	HY3	AAD+BLDfDIAG+FEMALE+firstHY2	
	PRECEPT	surv	HYPOSMIA	AAD+AADsq+BLDfDIAG+LEVODOPA+FEMALE+firstHY2	
	PRECEPT	surv	INS	AAD+BLDfDIAG+FEMALE	
	PRECEPT	surv	MOTORFLUX	AAD+AADsq+AGONIST+BLDfDIAG+LEVODOPA+FEMALE	
	PRECEPT	surv	SEADL70	AAD+AADsq+BLDfDIAG+FEMALE+firstHY2	
	PRECEPT	surv	SLEEP	AAD+BLDfDIAG+LEVODOPA+FEMALE+firstHY2	
	PROPARK	base	CONST	AAD+AGONIST+BLDfDIAG+FEMALE	
	PROPARK	base	COGi	AAD+BLDfDIAG+FEMALE+YEARS EDUC+firstHY2	
	PROPARK	base	DEPR	AAD+BLDfDIAG+FEMALE	
	PROPARK	base	DYSKINESIAS	AAD+AGONIST+BLDfDIAG+LEVODOPA+FEMALE+YEARS EDUC	
	PROPARK	base	HY3	AAD+BLDfDIAG+BLDfDIAGsq+FEMALE+firstHY2	
	PROPARK	base	HYPOSMIA	AAD+BLDfDIAG+LEVODOPA+FEMALE	
	PROPARK	base	INS	AAD+AGONIST+BLDfDIAG+LEVODOPA+FEMALE	
	PROPARK	base	MOTORFLUX	AAD+AGONIST+BLDfDIAG+LEVODOPA+DRT+FEMALE+YEARS EDUC	
	PROPARK	base	SLEEP	AAD+AGONIST+BLDfDIAG+LEVODOPA+FEMALE	
	PROPARK	cont	HY	AAD+AGONIST+LEVODOPA+FEMALE+YEARS EDUC+YEARfDIAG	
	PROPARK	cont	MMSE	AAD+AGONIST+FEMALE+YEARS EDUC+YEARfDIAG+YEARfDIAGsq	
	PROPARK	surv	CONST	AAD+AADsq+BLDfDIAG+FEMALE+firstHY2	
	PROPARK	surv	COGi	AAD+BLDfDIAG+BLDfDIAGsq+LEVODOPA+DRT+FEMALE+YEARS EDUC	
	PROPARK	surv	DEPR	AAD+AADsq+BLDfDIAG+FEMALE	
	PROPARK	surv	DYSKINESIAS	AAD+BLDfDIAG+BLDfDIAGsq+LEVODOPA+DRT+FEMALE	
	PROPARK	surv	HY3	AAD+AGONIST+BLDfDIAG+FEMALE	
	PROPARK	surv	INS	AAD+AADsq+BLDfDIAG+BLDfDIAGsq+DRT+FEMALE	
	PROPARK	surv	MOTORFLUX	AAD+BLDfDIAG+LEVODOPA+DRT+FEMALE	
	PROPARK	surv	SLEEP	AAD+BLDfDIAG+FEMALE	

base, logistic regression model at the baseline; surv, Cox survival model; cont, linear mixed effect model

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Supplemental Table 3 Study specific genomic inflation factor (lambda)

Phenotype	Lambda
base_CONST	0.982
base_COGi	0.965
base_DEPR	0.980
base_DYSKINESIAS	0.960
base_HY3	0.969
base_HYPOSMIA	0.965
base_INS	0.969
base_MOTORFLUX	0.960
base_SLEEP	0.952
cont_HY	0.997
cont_MMSE	1.005
cont_MOCA	1.031
cont_SEADL	1.015
cont_UPDRS1_scaled	1.030
cont_UPDRS2_scaled	1.014
cont_UPDRS3_scaled	1.020
cont_UPDRS4_scaled	1.018
cont_UPDRS_scaled	1.000
surv_COGi	1.003
surv_DEPR	0.986
surv_DYSKINESIAS	1.014
surv_HY3	1.005
surv_INS	0.995
surv_MOTORFLUX	1.007
surv_SEADL70	0.997

base, logistic regression model at the baseline; surv, Cox survival model; cont, linear mixed effect model
CONST, constipation; COGi, cognitive impairment; INS, insomnia; SLEEP, daytime sleepiness; MOTORFLUX, motor
fluctuations; HY3, Hoehn Yahr scale 3 or greater; RBD, REM sleep behavior disorder; DEPR, depression; MMSE, Mini
Mental State Examina-tion; Montreal Cognitive Assessment, SEADL, Schwab and England Activities of Daily Living Scale;
UPDRS, Unified Parkinson Disease Rating Scale; MDS-UPDRS, Movment Disorder Society revised version of UPDRS.

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Supplemental Table 4 Risk associated variance and the results of meta-analysis																		
SNP	dbSNP	A1	A2	A1 Freq	FrqSE Outcome	Analysis	N	Beta	SE	95% CI	Isq	Qtest	p	p<0.05	p<0.05/25	p<0.05/88	p<0.05/2022	NearGene
1:155135036	rs35749011	a	g	0.0291	0.0119 COGI	COGI_surv	2244	0.895	0.203	2.45 [1.64, 3.65]	0.00	0.794	1.06E-05	1	1	1	1	1 KRTCAP2
1:155135036	rs35749011	a	g	0.0259	0.0067 MOCA	MOCA_cont	1074	-1.164	0.373	-1.16 [-1.89, -0.43]	0.00	0.490	1.80E-03	1	1	1	1	0 KRTCAP2
1:155135036	rs35749011	a	g	0.0310	0.0131 COGI	COGI_base	2859	0.678	0.220	1.97 [1.28, 3.03]	0.00	0.848	2.02E-03	1	1	1	1	0 KRTCAP2
1:155135036	rs35749011	a	g	0.0289	0.0113 HY	HY_cont	3627	0.076	0.028	0.08 [0.02, 0.13]	0.00	0.531	7.10E-03	1	1	1	1	0 KRTCAP2
1:155135036	rs35749011	a	g	0.0263	0.0080 SEADL	SEADL_cont	2218	-1.641	0.748	-1.64 [-3.11, -0.18]	0.00	0.441	2.82E-02	1	1	1	1	0 KRTCAP2
1:155135036	rs35749011	a	g	0.0223	0.0076 UPDRS2_scaled	UPDRS2_scaled_cont	2103	0.212	0.099	0.21 [0.02, 0.41]	0.00	0.879	3.32E-02	1	1	1	1	0 KRTCAP2
1:155135036	rs35749011	a	g	0.0288	0.0156 DYSKINESIAS	DYSKINESIAS_base	1232	0.643	0.307	1.90 [1.04, 3.47]	25.50	0.261	3.66E-02	1	1	1	1	0 KRTCAP2
1:155135036	rs35749011	a	g	0.0265	0.0099 UPDRS_scaled	UPDRS_scaled_cont	2994	0.153	0.076	0.15 [0.00, 0.30]	0.00	0.855	4.50E-02	1	1	1	1	0 KRTCAP2
1:155135036	rs35749011	a	g	0.0274	0.0139 INS	INS_base	2103	0.364	0.218	1.44 [0.94, 2.21]	0.00	0.493	9.48E-02	1	1	1	1	0 KRTCAP2
1:155135036	rs35749011	a	g	0.0230	0.0075 UPDRS1_scaled	UPDRS1_scaled_cont	2111	0.157	0.099	0.16 [-0.04, 0.35]	0.00	0.704	1.15E-01	1	1	1	1	0 KRTCAP2
1:155135036	rs35749011	a	g	0.0346	0.0161 HY3	HY3_base	1289	0.440	0.315	1.55 [0.84, 2.88]	0.00	0.469	1.63E-01	1	1	1	1	0 KRTCAP2
1:155135036	rs35749011	a	g	0.0238	0.0119 MMSE	MMSE_cont	2114	-0.211	0.155	-0.21 [-0.52, 0.09]	0.00	0.850	1.74E-01	1	1	1	1	0 KRTCAP2
1:155135036	rs35749011	a	g	0.0244	0.0075 UPDRS3_scaled	UPDRS3_scaled_cont	2446	0.116	0.085	0.12 [-0.05, 0.28]	12.20	0.335	1.76E-01	1	1	1	1	0 KRTCAP2
1:155135036	rs35749011	a	g	0.0332	0.0158 DEPR	DEPR_surv	1314	0.301	0.229	1.35 [0.86, 2.12]	38.30	0.150	1.89E-01	1	1	1	1	0 KRTCAP2
1:155135036	rs35749011	a	g	0.0267	0.0092 HY3	HY3_surv	2582	0.212	0.192	1.24 [0.85, 1.80]	0.00	0.402	2.70E-01	1	1	1	1	0 KRTCAP2
1:155135036	rs35749011	a	g	0.0297	0.0140 SLEEP	SLEEP_base	1724	0.245	0.237	1.28 [0.80, 2.03]	7.00	0.375	3.00E-01	1	1	1	1	0 KRTCAP2
1:155135036	rs35749011	a	g	0.0298	0.0139 MOTORFLUX	MOTORFLUX_base	1803	0.247	0.250	1.28 [0.78, 2.09]	0.00	0.619	3.25E-01	1	1	1	1	0 KRTCAP2
1:155135036	rs35749011	a	g	0.0254	0.0088 DYSKINESIAS	DYSKINESIAS_surv	1656	0.170	0.183	1.19 [0.83, 1.70]	0.00	0.956	3.51E-01	1	1	1	1	0 KRTCAP2
1:155135036	rs35749011	a	g	0.0292	0.0137 HYPOSMIA	HYPOSMIA_base	1588	0.198	0.245	1.22 [0.75, 1.97]	0.00	0.657	4.19E-01	1	1	1	1	0 KRTCAP2
1:155135036	rs35749011	a	g	0.0243	0.0081 UPDRS4_scaled	UPDRS4_scaled_cont	1798	0.067	0.084	0.07 [-0.10, 0.23]	29.60	0.213	4.28E-01	1	1	1	1	0 KRTCAP2
1:155135036	rs35749011	a	g	0.0235	0.0058 SEADL70	SEADL70_surv	1277	0.203	0.292	1.23 [0.69, 2.17]	0.00	0.567	4.86E-01	1	1	1	1	0 KRTCAP2
1:155135036	rs35749011	a	g	0.0273	0.0082 MOTORFLUX	MOTORFLUX_surv	1709	0.034	0.153	1.03 [0.77, 1.40]	0.00	0.813	8.24E-01	1	1	1	1	0 KRTCAP2
1:155135036	rs35749011	a	g	0.0298	0.0145 CONST	CONST_base	1472	0.040	0.238	1.04 [0.65, 1.66]	0.00	0.729	8.65E-01	1	1	1	1	0 KRTCAP2
1:155135036	rs35749011	a	g	0.0268	0.0132 DEPR	DEPR_base	1870	-0.003	0.302	1.00 [0.55, 1.80]	0.00	0.724	9.92E-01	1	1	1	1	0 KRTCAP2
2:18147848	rs76116224	a	t	0.9045	0.0153 SLEEP	SLEEP_base	1033	-0.765	0.195	0.47 [0.32, 0.68]	0.00	0.453	8.41E-01	1	1	1	1	0 KCNS3
2:18147848	rs76116224	a	t	0.9038	0.0145 HY	HY_cont	2574	-0.048	0.021	-0.05 [-0.09, -0.01]	0.00	0.513	2.11E-02	1	1	1	1	0 KCNS3
2:18147848	rs76116224	a	t	0.9132	0.0094 SEADL70	SEADL70_surv	1100	-0.357	0.218	0.70 [0.46, 1.07]	0.00	0.702	1.01E-01	1	1	1	1	0 KCNS3
2:18147848	rs76116224	a	t	0.9049	0.0148 INS	INS_base	1529	-0.207	0.162	0.81 [0.59, 1.12]	45.70	0.101	2.01E-01	1	1	1	1	0 KCNS3
2:18147848	rs76116224	a	t	0.8977	0.0094 UPDRS3_scaled	UPDRS3_scaled_cont	1389	-0.089	0.073	-0.09 [-0.23, 0.05]	55.80	0.060	2.22E-01	1	1	1	1	0 KCNS3
2:18147848	rs76116224	a	t	0.8983	0.0131 UPDRS4_scaled	UPDRS4_scaled_cont	1091	0.091	0.081	0.09 [-0.07, 0.25]	0.00	0.425	2.59E-01	1	1	1	1	0 KCNS3
2:18147848	rs76116224	a	t	0.9010	0.0112 COGI	COGI_base	2369	-0.205	0.184	0.81 [0.57, 1.17]	0.00	0.708	2.63E-01	1	1	1	1	0 KCNS3
2:18147848	rs76116224	a	t	0.9062	0.0130 HY3	HY3_surv	1991	-0.138	0.126	0.87 [0.68, 1.12]	49.40	0.065	2.74E-01	1	1	1	1	0 KCNS3
2:18147848	rs76116224	a	t	0.8983	0.0135 UPDRS1_scaled	UPDRS1_scaled_cont	1092	-0.107	0.102	-0.11 [-0.31, 0.09]	39.80	0.173	2.91E-01	1	1	1	1	0 KCNS3
2:18147848	rs76116224	a	t	0.9053	0.0186 UPDRS_scaled	UPDRS_scaled_cont	1941	-0.065	0.064	-0.06 [-0.19, 0.06]	36.20	0.152	3.14E-01	1	1	1	1	0 KCNS3
2:18147848	rs76116224	a	t	0.9117	0.0128 COGI	COGI_surv	1672	0.111	0.181	1.12 [0.78, 1.59]	0.00	0.590	5.38E-01	1	1	1	1	0 KCNS3
2:18147848	rs76116224	a	t	0.9036	0.0090 DYSKINESIAS	DYSKINESIAS_surv	1115	0.089	0.161	1.09 [0.80, 1.50]	0.00	0.475	5.79E-01	1	1	1	1	0 KCNS3
2:18147848	rs76116224	a	t	0.9039	0.0126 DEPR	DEPR_base	1119	-0.110	0.244	0.90 [0.56, 1.44]	0.00	0.713	6.53E-01	1	1	1	1	0 KCNS3
2:18147848	rs76116224	a	t	0.9132	0.0180 SEADL	SEADL_cont	1200	0.271	0.623	0.27 [-0.95, 1.49]	0.00	0.501	6.64E-01	1	1	1	1	0 KCNS3
2:18147848	rs76116224	a	t	0.9205	0.0174 MMSE	MMSE_cont	1565	0.046	0.109	0.05 [-0.17, 0.26]	0.00	0.984	6.70E-01	1	1	1	1	0 KCNS3
2:18147848	rs76116224	a	t	0.8996	0.0128 UPDRS2_scaled	UPDRS2_scaled_cont	1087	0.032	0.100	0.03 [-0.17, 0.23]	0.00	0.648	7.53E-01	1	1	1	1	0 KCNS3
2:18147848	rs76116224	a	t	0.9019	0.0073 MOTORFLUX	MOTORFLUX_base	1112	-0.045	0.218	0.96 [0.62, 1.46]	0.00	0.684	8.36E-01	1	1	1	1	0 KCNS3
12:40614434	rs76904798	t	c	0.1552	0.0187 HY3	HY3_surv	2582	0.281	0.078	1.32 [1.14, 1.54]	17.90	0.283	3.01E-04	1	1	1	1	0 LRRK2
12:40614434	rs76904798	t	c	0.1450	0.0114 DYSKINESIAS	DYSKINESIAS_surv	1856	0.179	0.078	1.20 [1.03, 1.39]	0.00	0.456	2.12E-02	1	1	1	1	0 LRRK2
12:40614434	rs76904798	t	c	0.1553	0.0172 MMSE	MMSE_cont	2114	0.139	0.060	0.14 [0.02, 0.26]	0.00	0.936	2.12E-02	1	1	1	1	0 LRRK2
12:40614434	rs76904798	t	c	0.1460	0.0158 HYPOSMIA	HYPOSMIA_base	1588	0.207	0.115	1.23 [0.98, 1.54]	0.00	0.566	7.05E-02	1	1	1	1	0 LRRK2
12:40614434	rs76904798	t	c	0.1522	0.0165 HY	HY_cont	3627	0.020	0.012	0.02 [-0.00, 0.04]	14.40	0.303	1.02E-01	1	1	1	1	0 LRRK2
12:40614434	rs76904798	t	c	0.1458	0.0153 UPDRS1_scaled	UPDRS1_scaled_cont	2111	-0.064	0.040	-0.06 [-0.14, 0.01]	0.00	0.657	1.05E-01	1	1	1	1	0 LRRK2
12:40614434	rs76904798	t	c	0.1472	0.0206 MOCA	MOCA_cont	1074	0.268	0.166	0.27 [-0.06, 0.59]	33.90	0.209	1.07E-01	1	1	1	1	0 LRRK2
12:40614434	rs76904798	t	c	0.1540	0.0259 COGI	COGI_surv	2244	-0.145	0.104	0.87 [0.71, 1.06]	0.00	0.792	1.64E-01	1	1	1	1	0 LRRK2
12:40614434	rs76904798	t	c	0.1508	0.0123 DEPR	DEPR_surv	1314	-0.122	0.108	0.88 [0.72, 1.09]	0.00	0.485	2.59E-01	1	1	1	1	0 LRRK2
12:40614434	rs76904798	t	c	0.1521	0.0119 MOTORFLUX	MOTORFLUX_base	1803	0.120	0.110	1.13 [0.91, 1.40]	18.80	0.295	2.76E-01	1	1	1	1	0 LRRK2
12:40614434	rs76904798	t	c	0.1479	0.0189 MOTORFLUX	MOTORFLUX_surv	1709	0.060	0.066	1.06 [0.93, 1.21]	0.00	0.513	3.68E-01	1	1	1	1	0 LRRK2
12:40614434	rs76904798	t	c	0.1453	0.0158 UPDRS2_scaled	UPDRS2_scaled_cont	2103	-0.032	0.040	-0.03 [-0.11, 0.05]	0.00	0.484	4.16E-01	1	1	1	1	0 LRRK2
12:40614434	rs76904798	t	c	0.1569	0.0225 INS	INS_surv	1112	0.064	0.059	1.07 [0.89, 1.27]	0.00	0.464	4.75E-01	1	1	1	1	0 LRRK2
12:40614434	rs76904798	t	c	0.1555	0.0138 HY3	HY3_base	1289	-0.112	0.159	0.89 [0.66, 1.22]	9.20	0.333	4.81E-01	1	1	1	1	0 LRRK2
12:40614434	rs76904798	t	c	0.1490	0.0197 UPDRS_scaled	UPDRS_scaled_cont	2994	0.022	0.032	0.02 [-0.04, 0.09]	0.00	0.457	4.86E-01	1	1	1	1	0 LRRK2
12:40614434	rs76904798	t	c	0.1463	0.0166 UPDRS4_scaled	UPDRS4_scaled_cont	1798	0.022	0.035	0.02 [-0.05, 0.09]	0.00	0.958	5.17E-01	1	1	1	1	0 LRRK2
12:40614434	rs76904798	t	c	0.1574	0.0197 DEPR	DEPR_base	2138	0.077	0.121	1.08 [0.85, 1.37]	0.00	0.648	5.27E-01	1	1	1	1	0 LRRK2
12:40614434	rs76904798	t	c	0.1539	0.0210 INS	INS_base	2220	-0.052	0.097	0.95 [0.79, 1.15]	14.60	0.316	5.95E-01	1	1	1	1	0 LRRK2
12:40614434	rs76904798	t	c	0.1531	0.0131 DYSKINESIAS	DYSKINESIAS_base	1232	0.072	0.137	1.07 [0.82, 1.41]	5.90	0.346	5.98E-01	1	1	1	1	0 LRRK2
12:40614434	rs76904798	t	c	0.1536	0.0122 CONST	CONST_base	1472	-0.059	0.117	0.94 [0.75, 1.19]	0.00	0.647	6.12E-01	1	1	1	1	0 LRRK2
12:40614434																		

1	8:11712443	rs1293298	a	c	0.7418	0.0069	DYSKINESIAS	DYSKINESIAS_base	1232	0.032	0.117	1.03 [0.82, 1.30]	0.00	0.710	7.86E-01	1	0	0	0	CTSB
2	8:11712443	rs1293298	a	c	0.7461	0.0096	MOTORFLUX	MOTORFLUX_base	1803	-0.010	0.094	0.99 [0.82, 1.19]	0.00	0.751	9.12E-01	0	0	0	0	CTSB
	8:11712443	rs1293298	a	c	0.7511	0.0114	SEADL	SEADL_cont	2218	-0.027	0.265	-0.03 [-0.55, 0.49]	6.20	0.382	9.19E-01	0	0	0	0	CTSB
3	8:11712443	rs1293298	a	c	0.7459	0.0100	MOTORFLUX	MOTORFLUX_surv	1709	0.004	0.055	1.00 [0.90, 1.12]	0.00	0.683	9.46E-01	0	0	0	0	CTSB
	8:11712443	rs1293298	a	c	0.7519	0.0167	HY	HY_cont	3627	0.001	0.010	0.00 [-0.02, 0.02]	0.00	0.654	9.51E-01	0	0	0	0	CTSB
4	16:50736656	rs6500328	a	g	0.6003	0.0206	SLEEP	SLEEP_base	1724	-0.272	0.085	0.76 [0.64, 0.90]	0.00	0.459	1.45E-03	0	0	0	0	NOD2
	16:50736656	rs6500328	a	g	0.6013	0.0151	MOCA	MOCA_cont	1074	0.333	0.149	0.33 [0.04, 0.63]	37.50	0.187	2.56E-02	0	0	0	0	NOD2
5	16:50736656	rs6500328	a	g	0.6035	0.0139	SEADL	SEADL_cont	2218	-0.510	0.262	-0.51 [-1.02, 0.00]	28.00	0.205	5.19E-02	0	0	0	0	NOD2
	16:50736656	rs6500328	a	g	0.6086	0.0137	DEPR	DEPR_base	2138	-0.143	0.090	0.87 [0.73, 1.03]	0.00	0.995	1.12E-01	0	0	0	0	NOD2
6	16:50736656	rs6500328	a	g	0.5790	0.0186	INS	INS_surv	1112	-0.116	0.076	0.89 [0.77, 1.03]	16.80	0.305	1.24E-01	0	0	0	0	NOD2
	16:50736656	rs6500328	a	g	0.6009	0.0197	INS	INS_base	2220	-0.091	0.071	0.91 [0.80, 1.05]	0.00	0.724	1.98E-01	0	0	0	0	NOD2
7	16:50736656	rs6500328	a	g	0.6069	0.0100	MOTORFLUX	MOTORFLUX_base	1803	-0.097	0.083	0.91 [0.77, 1.07]	57.10	0.053	2.42E-01	0	0	0	0	NOD2
	16:50736656	rs6500328	a	g	0.6068	0.0147	DEPR	DEPR_surv	1314	-0.104	0.096	0.90 [0.75, 1.09]	36.30	0.165	2.78E-01	0	0	0	0	NOD2
8	16:50736656	rs6500328	a	g	0.6091	0.0137	UPDRS1_scaled	UPDRS1_scaled_cont	2111	-0.039	0.037	-0.04 [-0.11, 0.03]	0.00	0.658	2.91E-01	0	0	0	0	NOD2
	16:50736656	rs6500328	a	g	0.6147	0.0187	UPDRS_scaled	UPDRS_scaled_cont	2994	-0.024	0.028	-0.02 [-0.08, 0.03]	46.00	0.054	3.83E-01	0	0	0	0	NOD2
9	16:50736656	rs6500328	a	g	0.6093	0.0137	UPDRS2_scaled	UPDRS2_scaled_cont	2103	0.024	0.038	0.02 [-0.05, 0.10]	40.90	0.118	5.22E-01	0	0	0	0	NOD2
	16:50736656	rs6500328	a	g	0.6057	0.0094	DYSKINESIAS	DYSKINESIAS_base	1232	0.062	0.102	1.06 [0.87, 1.30]	0.00	0.654	5.45E-01	0	0	0	0	NOD2
10	16:50736656	rs6500328	a	g	0.5942	0.0185	DYSKINESIAS	DYSKINESIAS_surv	1856	0.039	0.074	1.04 [0.90, 1.20]	46.50	0.082	5.97E-01	0	0	0	0	NOD2
	16:50736656	rs6500328	a	g	0.5894	0.0260	HY3	HY3_surv	2582	0.035	0.071	1.04 [0.90, 1.19]	33.20	0.152	6.16E-01	0	0	0	0	NOD2
11	16:50736656	rs6500328	a	g	0.6016	0.0169	MMSE	MMSE_cont	2114	-0.023	0.048	-0.02 [-0.12, 0.07]	32.60	0.168	6.34E-01	0	0	0	0	NOD2
	16:50736656	rs6500328	a	g	0.5990	0.0289	MOTORFLUX	MOTORFLUX_surv	1709	0.026	0.060	1.03 [0.91, 1.15]	0.00	0.972	6.61E-01	0	0	0	0	NOD2
12	16:50736656	rs6500328	a	g	0.6056	0.0182	COGI	COGI_base	2859	-0.039	0.088	0.96 [0.81, 1.14]	0.00	0.607	6.61E-01	0	0	0	0	NOD2
	16:50736656	rs6500328	a	g	0.5938	0.0216	CONST	CONST_base	1472	-0.034	0.087	0.97 [0.81, 1.15]	52.40	0.078	7.00E-01	0	0	0	0	NOD2
13	16:50736656	rs6500328	a	g	0.6053	0.0142	UPDRS3_scaled	UPDRS3_scaled_cont	2446	-0.012	0.032	-0.01 [-0.07, 0.05]	45.00	0.079	7.12E-01	0	0	0	0	NOD2
	16:50736656	rs6500328	a	g	0.6073	0.0230	HY	HY_cont	3627	-0.003	0.010	-0.00 [-0.02, 0.02]	26.70	0.182	7.39E-01	0	0	0	0	NOD2
14	16:50736656	rs6500328	a	g	0.6019	0.0122	HY3	HY3_base	1289	-0.035	0.119	0.97 [0.76, 1.22]	0.00	0.446	7.68E-01	0	0	0	0	NOD2
	16:50736656	rs6500328	a	g	0.5948	0.0224	SEADL70	SEADL70_surv	1683	-0.021	0.105	0.98 [0.80, 1.20]	0.00	0.519	8.42E-01	0	0	0	0	NOD2
15	16:50736656	rs6500328	a	g	0.6081	0.0143	UPDRS4_scaled	UPDRS4_scaled_cont	1798	0.006	0.033	0.01 [-0.06, 0.07]	1.50	0.407	8.49E-01	0	0	0	0	NOD2
	16:50736656	rs6500328	a	g	0.5950	0.0213	HYPOSIMIA	HYPOSIMIA_base	1588	-0.009	0.082	0.99 [0.84, 1.16]	0.00	0.506	9.09E-01	0	0	0	0	NOD2
16	12:133063768	rs11610045	a	g	0.4962	0.0263	MMSE	MMSE_cont	2114	0.137	0.044	1.04 [0.05, 0.22]	25.40	0.226	1.79E-03	0	0	0	0	FBRSL1
	12:133063768	rs11610045	a	g	0.4840	0.0236	DYSKINESIAS	DYSKINESIAS_surv	1856	0.138	0.057	1.15 [1.03, 1.28]	0.00	0.513	1.50E-02	0	0	0	0	FBRSL1
17	12:133063768	rs11610045	a	g	0.5042	0.0295	COGI	COGI_base	2859	-0.185	0.085	0.83 [0.70, 0.98]	24.80	0.231	3.01E-02	0	0	0	0	FBRSL1
	12:133063768	rs11610045	a	g	0.4976	0.0303	HY3	HY3_base	1289	0.213	0.114	1.24 [0.99, 1.55]	61.90	0.073	6.09E-02	0	0	0	0	FBRSL1
18	12:133063768	rs11610045	a	g	0.5054	0.0337	HY	HY_cont	3627	-0.015	0.009	-0.02 [-0.03, 0.00]	11.70	0.330	7.90E-02	0	0	0	0	FBRSL1
	12:133063768	rs11610045	a	g	0.4949	0.0128	SEADL	SEADL_cont	2218	0.372	0.232	0.37 [-0.08, 0.83]	29.20	0.195	1.09E-01	0	0	0	0	FBRSL1
19	12:133063768	rs11610045	a	g	0.4881	0.0229	UPDRS4_scaled	UPDRS4_scaled_cont	1798	0.036	0.025	0.04 [-0.01, 0.08]	0.00	0.655	1.46E-01	0	0	0	0	FBRSL1
	12:133063768	rs11610045	a	g	0.4866	0.0219	UPDRS1_scaled	UPDRS1_scaled_cont	2111	-0.039	0.029	-0.04 [-0.10, 0.02]	3.60	0.399	1.69E-01	0	0	0	0	FBRSL1
20	12:133063768	rs11610045	a	g	0.4848	0.0230	INS	INS_surv	1112	-0.086	0.062	0.92 [0.81, 1.04]	0.00	0.497	1.70E-01	0	0	0	0	FBRSL1
	12:133063768	rs11610045	a	g	0.5026	0.0265	DEPR	DEPR_surv	1314	-0.096	0.075	0.91 [0.79, 1.05]	0.00	0.931	2.00E-01	0	0	0	0	FBRSL1
21	12:133063768	rs11610045	a	g	0.5169	0.0384	HY3	HY3_surv	2582	-0.078	0.062	0.93 [0.82, 1.04]	31.10	0.170	2.11E-01	0	0	0	0	FBRSL1
	12:133063768	rs11610045	a	g	0.5000	0.0353	UPDRS3_scaled	UPDRS3_scaled_cont	2446	-0.031	0.026	-0.03 [-0.08, 0.02]	5.80	0.386	2.26E-01	0	0	0	0	FBRSL1
22	12:133063768	rs11610045	a	g	0.4815	0.0284	DYSKINESIAS	DYSKINESIAS_base	1232	0.118	0.099	1.12 [0.93, 1.36]	0.00	0.795	2.33E-01	0	0	0	0	FBRSL1
	12:133063768	rs11610045	a	g	0.4862	0.0227	UPDRS2_scaled	UPDRS2_scaled_cont	2103	-0.032	0.029	-0.03 [-0.09, 0.02]	38.00	0.139	2.57E-01	0	0	0	0	FBRSL1
23	12:133063768	rs11610045	a	g	0.4874	0.0266	MOTORFLUX	MOTORFLUX_base	1803	0.081	0.080	1.08 [0.93, 1.27]	0.00	0.811	3.13E-01	0	0	0	0	FBRSL1
	12:133063768	rs11610045	a	g	0.4949	0.0276	COGI	COGI_surv	2244	-0.066	0.074	0.94 [0.81, 1.08]	25.80	0.214	3.73E-01	0	0	0	0	FBRSL1
24	12:133063768	rs11610045	a	g	0.4943	0.0121	SEADL70	SEADL70_surv	1683	-0.080	0.092	0.92 [0.77, 1.11]	32.00	0.208	3.89E-01	0	0	0	0	FBRSL1
	12:133063768	rs11610045	a	g	0.5006	0.0308	UPDRS_scaled	UPDRS_scaled_cont	2994	-0.019	0.023	-0.02 [-0.06, 0.03]	22.80	0.233	4.18E-01	0	0	0	0	FBRSL1
25	12:133063768	rs11610045	a	g	0.4994	0.0238	HYPOSIMIA	HYPOSIMIA_base	1588	0.040	0.079	1.04 [0.89, 1.21]	0.00	0.416	6.09E-01	0	0	0	0	FBRSL1
	12:133063768	rs11610045	a	g	0.4859	0.0228	MOTORFLUX	MOTORFLUX_surv	1709	-0.014	0.048	0.99 [0.90, 1.08]	0.00	0.793	7.68E-01	0	0	0	0	FBRSL1
26	1:161469054	rs6658353	c	g	0.5212	0.0110	HY3	HY3_base	1289	-0.365	0.117	0.69 [0.55, 0.87]	0.00	0.712	1.85E-03	0	0	0	0	FCGR2A
	1:161469054	rs6658353	c	g	0.5130	0.0256	UPDRS1_scaled	UPDRS1_scaled_cont	2111	0.043	0.029	0.04 [-0.01, 0.10]	0.00	0.952	1.36E-01	0	0	0	0	FCGR2A
27	1:161469054	rs6658353	c	g	0.5249	0.0186	HYPOSIMIA	HYPOSIMIA_surv	1588	0.111	0.080	1.12 [0.96, 1.31]	2.30	0.402	1.64E-01	0	0	0	0	FCGR2A
	1:161469054	rs6658353	c	g	0.5121	0.0208	DYSKINESIAS	DYSKINESIAS_base	1856	-0.077	0.058	0.93 [0.83, 1.04]	0.00	0.674	1.85E-01	0	0	0	0	FCGR2A
28	1:161469054	rs6658353	c	g	0.5102	0.0303	MOCA	MOCA_cont	1074	-0.156	0.119	-0.16 [-0.39, 0.08]	0.00	0.780	1.91E-01	0	0	0	0	FCGR2A
	1:161469054	rs6658353	c	g	0.5197	0.0233	COGI	COGI_base	2859	0.103	0.086	1.11 [0.94, 1.31]	0.00	0.749	2.31E-01	0	0	0	0	FCGR2A
29	1:161469054	rs6658353	c	g	0.5167	0.0267	UPDRS_scaled	UPDRS_scaled_cont	2994	-0.028	0.023	-0.03 [-0.07, 0.02]	0.00	0.689	2.38E-01	0	0	0	0	FCGR2A
	1:161469054	rs6658353	c	g	0.5136	0.0240	DEPR	DEPR_surv	1314	0.085	0.080	1.09 [0.93, 1.27]	18.10	0.296	2.88E-01	0	0	0	0	FCGR2A
30	1:161469054	rs6658353	c	g	0.5296	0.0246	HY3	HY3_surv	2582	-0.059	0.061	0.94 [0.84, 1.06]	0.00	0.443	3.36E-01	0	0	0	0	FCGR2A
	1:161469054	rs6658353	c	g	0.5096	0.0290	MMSE	MMSE_cont	2114	-0.034	0.044	-0.03 [-0.12, 0.05]	0.00	0.881	4.38E-01	0	0	0	0	FCGR2A
31	1:161469054	rs6658353	c	g	0.5088	0.0244	MOTORFLUX	MOTORFLUX_surv	1709	0.038	0.051	1.04 [0.94, 1.15]	0.00	0.907	4.55E-01	0	0	0	0	FCGR2A
	1:161469054	rs6658353	c	g	0.5229	0.0206	INS	INS_base	2220	0.047	0.069	1.05 [0.91, 1.20]	0.00	0.940						

1	6:72487762	rs12528068	t	c	0.2920	0.0195	UPDRS4_scaled	UPDRS4_scaled_cont	1798	0.003	0.028	0.00 [-0.05, 0.06]	54.30	0.053	9.21E-01	0	0	0	0	RIMS1
2	6:72487762	rs12528068	t	c	0.2906	0.0097	MOTORFLUX	MOTORFLUX_base	1803	-0.008	0.092	0.99 [0.83, 1.19]	0.00	0.591	9.33E-01	0	0	0	0	RIMS1
3	6:72487762	rs12528068	t	c	0.2937	0.0136	INS	INS_base	2220	-0.002	0.078	1.00 [0.86, 1.16]	22.60	0.250	9.80E-01	0	0	0	0	RIMS1
4	1:23266461	rs10797576	t	c	0.1416	0.0080	MOTORFLUX	MOTORFLUX_base	1803	0.337	0.114	1.40 [1.12, 1.75]	0.00	0.943	3.01E-03	0	0	0	0	SIPA1L2
5	1:23266461	rs10797576	t	c	0.1371	0.0119	COGI	COGI_base	2859	0.349	0.118	1.42 [1.12, 1.79]	4.40	0.396	3.16E-03	0	0	0	0	SIPA1L2
6	1:23266461	rs10797576	t	c	0.1482	0.0136	DYSKINESIAS	DYSKINESIAS_surv	1856	0.189	0.080	1.21 [1.03, 1.41]	0.00	0.640	1.75E-02	0	0	0	0	SIPA1L2
7	1:23266461	rs10797576	t	c	0.1408	0.0148	MOCA	MOCA_cont	1074	-0.383	0.175	-0.38 [-0.73, -0.04]	0.00	0.762	2.88E-02	0	0	0	0	SIPA1L2
8	1:23266461	rs10797576	t	c	0.1390	0.0144	CONST	CONST_base	1472	0.152	0.122	1.16 [0.92, 1.48]	0.00	0.566	2.14E-01	0	0	0	0	SIPA1L2
9	1:23266461	rs10797576	t	c	0.1381	0.0178	SLEEP	SLEEP_base	1724	0.133	0.121	1.14 [0.90, 1.45]	0.00	0.546	2.70E-01	0	0	0	0	SIPA1L2
10	1:23266461	rs10797576	t	c	0.1479	0.0182	UPDRS4_scaled	UPDRS4_scaled_cont	1798	0.035	0.035	0.03 [-0.03, 0.10]	0.00	0.591	3.28E-01	0	0	0	0	SIPA1L2
11	1:23266461	rs10797576	t	c	0.1399	0.0034	DYSKINESIAS	DYSKINESIAS_base	1232	-0.119	0.146	0.89 [0.67, 1.18]	0.00	0.996	4.14E-01	0	0	0	0	SIPA1L2
12	1:23266461	rs10797576	t	c	0.1379	0.0037	HY3	HY3_base	1289	-0.136	0.173	0.87 [0.62, 1.23]	34.00	0.220	4.31E-01	0	0	0	0	SIPA1L2
13	1:23266461	rs10797576	t	c	0.1360	0.0210	UPDRS_scaled	UPDRS_scaled_cont	2994	0.023	0.034	0.02 [-0.04, 0.09]	0.00	0.944	5.00E-01	0	0	0	0	SIPA1L2
14	1:23266461	rs10797576	t	c	0.1361	0.0217	HY	HY_cont	3627	0.008	0.013	0.01 [-0.02, 0.03]	3.10	0.414	5.25E-01	0	0	0	0	SIPA1L2
15	1:23266461	rs10797576	t	c	0.1440	0.0175	INS	INS_surv	1112	0.057	0.095	1.06 [0.88, 1.27]	16.00	0.311	5.47E-01	0	0	0	0	SIPA1L2
16	1:23266461	rs10797576	t	c	0.1408	0.0187	UPDRS3_scaled	UPDRS3_scaled_cont	2446	0.021	0.037	0.02 [-0.05, 0.09]	0.00	0.951	5.75E-01	0	0	0	0	SIPA1L2
17	1:23266461	rs10797576	t	c	0.1415	0.0198	COGI	COGI_surv	2244	0.057	0.111	1.06 [0.85, 1.32]	33.20	0.152	6.07E-01	0	0	0	0	SIPA1L2
18	1:23266461	rs10797576	t	c	0.1392	0.0168	HY3	HY3_surv	2582	0.048	0.094	1.05 [0.87, 1.26]	43.20	0.079	6.10E-01	0	0	0	0	SIPA1L2
19	1:23266461	rs10797576	t	c	0.1410	0.0162	HYPOSIMIA	HYPOSIMIA_base	1588	0.049	0.116	1.05 [0.84, 1.32]	15.10	0.317	6.71E-01	0	0	0	0	SIPA1L2
20	1:23266461	rs10797576	t	c	0.1297	0.0192	MMSE	MMSE_cont	2114	-0.027	0.066	-0.03 [-0.16, 0.10]	0.00	0.787	6.87E-01	0	0	0	0	SIPA1L2
21	1:23266461	rs10797576	t	c	0.1428	0.0201	UPDRS1_scaled	UPDRS1_scaled_cont	2111	-0.013	0.042	-0.01 [-0.09, 0.07]	29.00	0.207	7.57E-01	0	0	0	0	SIPA1L2
22	1:23266461	rs10797576	t	c	0.1393	0.0173	INS	INS_base	2220	-0.028	0.102	0.97 [0.80, 1.19]	0.00	0.498	7.86E-01	0	0	0	0	SIPA1L2
23	1:23266461	rs10797576	t	c	0.1446	0.0200	UPDRS2_scaled	UPDRS2_scaled_cont	2103	0.006	0.041	0.01 [-0.08, 0.09]	0.00	0.502	8.88E-01	0	0	0	0	SIPA1L2
24	1:23266461	rs10797576	t	c	0.1459	0.0118	SEADL70	SEADL70_surv	1683	-0.016	0.135	0.98 [0.76, 1.28]	13.60	0.327	9.05E-01	0	0	0	0	SIPA1L2
25	1:23266461	rs10797576	t	c	0.1379	0.0149	DEPR	DEPR_surv	1314	0.009	0.118	1.01 [0.80, 1.27]	37.90	0.154	9.42E-01	0	0	0	0	SIPA1L2
26	1:23266461	rs10797576	t	c	0.1393	0.0129	MOTORFLUX	MOTORFLUX_surv	1709	-0.005	0.072	0.99 [0.86, 1.15]	0.00	0.442	9.44E-01	0	0	0	0	SIPA1L2
27	1:23266461	rs10797576	t	c	0.1369	0.0172	DEPR	DEPR_base	2138	0.007	0.133	1.01 [0.78, 1.31]	0.00	0.569	9.60E-01	0	0	0	0	SIPA1L2
28	1:23266461	rs10797576	t	c	0.1351	0.0165	SEADL	SEADL_cont	2218	-0.012	0.344	-0.01 [-0.69, 0.66]	0.00	0.473	9.73E-01	0	0	0	0	SIPA1L2
29	4:17968811	rs34025766	a	t	0.1636	0.0118	DYSKINESIAS	DYSKINESIAS_surv	1856	0.224	0.077	1.25 [1.08, 1.45]	32.30	0.182	3.50E-03	0	0	0	0	LCORL
30	4:17968811	rs34025766	a	t	0.1598	0.0093	SEADL	SEADL_cont	2218	-0.758	0.312	-0.76 [-1.37, -0.15]	13.20	0.327	1.52E-02	0	0	0	0	LCORL
31	4:17968811	rs34025766	a	t	0.1645	0.0096	CONST	CONST_base	1472	0.271	0.116	1.31 [1.05, 1.64]	48.60	0.100	1.90E-02	0	0	0	0	LCORL
32	4:17968811	rs34025766	a	t	0.1581	0.0127	MMSE	MMSE_cont	2114	-0.129	0.060	-0.13 [-0.25, -0.01]	0.00	0.874	3.27E-02	0	0	0	0	LCORL
33	4:17968811	rs34025766	a	t	0.1617	0.0190	INS	INS_surv	1112	0.173	0.084	1.19 [1.01, 1.40]	0.00	0.648	3.83E-02	0	0	0	0	LCORL
34	4:17968811	rs34025766	a	t	0.1604	0.0189	COGI	COGI_surv	2244	0.201	0.098	1.22 [1.01, 1.48]	29.00	0.187	4.03E-02	0	0	0	0	LCORL
35	4:17968811	rs34025766	a	t	0.1601	0.0128	DEPR	DEPR_surv	1314	0.200	0.099	1.22 [1.01, 1.48]	0.00	0.904	4.38E-02	0	0	0	0	LCORL
36	4:17968811	rs34025766	a	t	0.1536	0.0222	HY	HY_cont	3627	0.022	0.012	0.02 [-0.00, 0.05]	33.60	0.122	6.29E-02	0	0	0	0	LCORL
37	4:17968811	rs34025766	a	t	0.1660	0.0106	UPDRS1_scaled	UPDRS1_scaled_cont	2111	0.062	0.037	0.06 [-0.01, 0.14]	0.00	0.541	9.60E-02	0	0	0	0	LCORL
38	4:17968811	rs34025766	a	t	0.1643	0.0078	SEADL70	SEADL70_surv	1683	0.129	0.118	1.14 [0.90, 1.43]	8.70	0.357	2.77E-01	0	0	0	0	LCORL
39	4:17968811	rs34025766	a	t	0.1574	0.0202	UPDRS_scaled	UPDRS_scaled_cont	2994	0.031	0.032	0.03 [-0.03, 0.09]	14.10	0.313	3.34E-01	0	0	0	0	LCORL
40	4:17968811	rs34025766	a	t	0.1685	0.0079	DYSKINESIAS	DYSKINESIAS_base	1232	0.124	0.131	1.13 [0.87, 1.46]	0.00	0.558	3.47E-01	0	0	0	0	LCORL
41	4:17968811	rs34025766	a	t	0.1634	0.0149	MOTORFLUX	MOTORFLUX_surv	1709	-0.060	0.065	0.94 [0.83, 1.07]	0.00	0.718	3.53E-01	0	0	0	0	LCORL
42	4:17968811	rs34025766	a	t	0.1518	0.0221	HY3	HY3_surv	2582	0.068	0.087	1.07 [0.90, 1.27]	43.70	0.076	4.37E-01	0	0	0	0	LCORL
43	4:17968811	rs34025766	a	t	0.1659	0.0111	UPDRS2_scaled	UPDRS2_scaled_cont	2103	0.027	0.037	0.03 [-0.05, 0.10]	30.80	0.193	4.65E-01	0	0	0	0	LCORL
44	4:17968811	rs34025766	a	t	0.1638	0.0091	DEPR	DEPR_base	2138	0.082	0.119	1.09 [0.86, 1.37]	0.00	0.681	4.91E-01	0	0	0	0	LCORL
45	4:17968811	rs34025766	a	t	0.1644	0.0108	SLEEP	SLEEP_base	1724	0.040	0.116	1.04 [0.83, 1.30]	26.30	0.228	7.30E-01	0	0	0	0	LCORL
46	4:17968811	rs34025766	a	t	0.1643	0.0124	HYPOSIMIA	HYPOSIMIA_base	1588	-0.035	0.108	0.97 [0.78, 1.19]	0.00	0.547	7.44E-01	0	0	0	0	LCORL
47	4:17968811	rs34025766	a	t	0.1571	0.0194	COGI	COGI_base	2859	-0.033	0.121	0.97 [0.76, 1.23]	27.90	0.206	7.87E-01	0	0	0	0	LCORL
48	4:17968811	rs34025766	a	t	0.1675	0.0073	MOTORFLUX	MOTORFLUX_base	1803	0.025	0.106	1.03 [0.83, 1.26]	0.00	0.906	8.14E-01	0	0	0	0	LCORL
49	4:17968811	rs34025766	a	t	0.1585	0.0239	UPDRS3_scaled	UPDRS3_scaled_cont	2446	-0.007	0.034	-0.01 [-0.07, 0.06]	33.40	0.162	8.47E-01	0	0	0	0	LCORL
50	4:17968811	rs34025766	a	t	0.1675	0.0104	UPDRS4_scaled	UPDRS4_scaled_cont	1798	0.005	0.032	0.01 [-0.06, 0.07]	0.00	0.925	8.71E-01	0	0	0	0	LCORL
51	4:17968811	rs34025766	a	t	0.1632	0.0107	HY3	HY3_base	1289	-0.024	0.157	0.98 [0.72, 1.33]	0.00	0.960	8.77E-01	0	0	0	0	LCORL
52	4:17968811	rs34025766	a	t	0.1657	0.0121	INS	INS_base	2220	-0.015	0.095	0.99 [0.82, 1.19]	48.40	0.060	8.79E-01	0	0	0	0	LCORL
53	19:2341047	rs55818311	t	c	0.6692	0.0133	DEPR	DEPR_base	2138	0.287	0.101	1.33 [1.09, 1.62]	0.00	0.701	4.49E-03	0	0	0	0	SPPL2B
54	19:2341047	rs55818311	t	c	0.6744	0.0188	COGI	COGI_base	2859	0.154	0.095	1.17 [0.97, 1.40]	1.00	0.421	1.04E-01	0	0	0	0	SPPL2B
55	19:2341047	rs55818311	t	c	0.6784	0.0154	INS	INS_surv	1112	-0.107	0.072	0.90 [0.78, 1.03]	0.00	0.550	1.36E-01	0	0	0	0	SPPL2B
56	19:2341047	rs55818311	t	c	0.6614	0.0103	MMSE	MMSE_cont	2114	-0.067	0.050	-0.07 [-0.16, 0.03]	0.00	0.628	1.80E-01	0	0	0	0	SPPL2B
57	19:2341047	rs55818311	t	c	0.6673	0.0181	UPDRS1_scaled	UPDRS1_scaled_cont	2111	0.037	0.034	0.04 [-0.03, 0.10]	11.60	0.341	2.71E-01	0	0	0	0	SPPL2B
58	19:2341047	rs55818311	t	c	0.6766	0.0149	CONST	CONST_base	1472	0.078	0.091	1.08 [0.90, 1.29]	0.00	0.745	3.92E-01	0	0	0	0	SPPL2B
59	19:2341047	rs55818311	t	c	0.6671	0.0199	UPDRS4_scaled	UPDRS4_scaled_cont	2994	-0.023	0.029	-0.02 [-0.08, 0.03]	0.00	0.691	4.26E-01	0	0	0	0	SPPL2B
60	19:2341047	rs55818311	t	c	0.6718	0.0208	UPDRS_scaled	UPDRS_scaled_cont	2994	0.021	0.027	0.02 [-0.03, 0.07]	28.90	0.179	4.30E-01	0	0	0	0	SPPL2B
61	19:2341047	rs55818311	t	c	0.6714	0.0														

1	9:17727065	rs10756907	a	g	0.7601	0.0166	MOCA	MOCA_cont	1074	-0.116	0.140	-0.12 [-0.39, 0.16]	43.70	0.149	4.07E-01	0	0	0	0	SH3GL2
2	9:17727065	rs10756907	a	g	0.7511	0.0212	HYPOSOMIA	HYPOSOMIA_base	1588	0.057	0.092	1.06 [0.88, 1.27]	33.10	0.188	5.33E-01	0	0	0	0	SH3GL2
3	9:17727065	rs10756907	a	g	0.7520	0.0226	DEPR	DEPR_base	2138	0.064	0.106	1.07 [0.87, 1.31]	23.40	0.243	5.46E-01	0	0	0	0	SH3GL2
4	9:17727065	rs10756907	a	g	0.7446	0.0262	UPDRS3_scaled	UPDRS3_scaled_cont	2446	0.017	0.030	0.02 [-0.04, 0.07]	0.00	0.617	5.74E-01	0	0	0	0	SH3GL2
5	9:17727065	rs10756907	a	g	0.7621	0.0142	SEADL70	SEADL70_surv	1683	-0.029	0.105	0.97 [0.79, 1.19]	0.00	0.672	7.85E-01	0	0	0	0	SH3GL2
6	9:17727065	rs10756907	a	g	0.7752	0.0154	DYSKINESIAS	DYSKINESIAS_base	1232	-0.022	0.120	0.98 [0.77, 1.24]	0.00	0.781	8.53E-01	0	0	0	0	SH3GL2
7	9:17727065	rs10756907	a	g	0.7565	0.0215	UPDRS_scaled	UPDRS_scaled_cont	2994	0.005	0.027	0.00 [-0.05, 0.06]	9.50	0.355	8.55E-01	0	0	0	0	SH3GL2
8	9:17727065	rs10756907	a	g	0.7606	0.0286	INS	INS_surv	1112	-0.014	0.078	0.99 [0.85, 1.15]	47.10	0.093	8.55E-01	0	0	0	0	SH3GL2
9	9:17727065	rs10756907	a	g	0.7507	0.0233	UPDRS4_scaled	UPDRS4_scaled_cont	1798	-0.004	0.029	-0.00 [-0.06, 0.05]	0.00	0.791	9.01E-01	0	0	0	0	SH3GL2
10	9:17727065	rs10756907	a	g	0.7679	0.0186	MOTORFLUX	MOTORFLUX_base	1803	-0.007	0.095	0.99 [0.82, 1.20]	0.00	0.976	9.46E-01	0	0	0	0	SH3GL2
11	13:49927732	rs9568188	t	c	0.7423	0.0204	DYSKINESIAS	DYSKINESIAS_base	1232	-0.307	0.117	0.74 [0.58, 0.93]	12.70	0.318	8.91E-03	0	0	0	0	CAB39L
12	13:49927732	rs9568188	t	c	0.7471	0.0080	SEADL70	SEADL70_surv	1683	-0.220	0.100	0.80 [0.66, 0.98]	0.00	0.585	2.82E-02	0	0	0	0	CAB39L
13	13:49927732	rs9568188	t	c	0.7482	0.0249	UPDRS2_scaled	UPDRS2_scaled_cont	2103	-0.062	0.034	-0.06 [-0.13, 0.00]	33.40	0.173	6.82E-02	0	0	0	0	CAB39L
14	13:49927732	rs9568188	t	c	0.7434	0.0236	MMSE	MMSE_cont	2114	0.092	0.051	0.09 [-0.01, 0.19]	0.00	0.826	7.36E-02	0	0	0	0	CAB39L
15	13:49927732	rs9568188	t	c	0.7479	0.0241	UPDRS4_scaled	UPDRS4_scaled_cont	1798	-0.035	0.029	-0.03 [-0.09, 0.02]	0.00	0.937	2.33E-01	0	0	0	0	CAB39L
16	13:49927732	rs9568188	t	c	0.7451	0.0290	DEPR	DEPR_base	2138	-0.114	0.104	0.89 [0.73, 1.09]	0.00	0.574	2.74E-01	0	0	0	0	CAB39L
17	13:49927732	rs9568188	t	c	0.7470	0.0176	COGi	COGi_surv	2244	-0.087	0.084	0.92 [0.78, 1.08]	0.00	0.758	2.99E-01	0	0	0	0	CAB39L
18	13:49927732	rs9568188	t	c	0.7489	0.0251	UPDRS1_scaled	UPDRS1_scaled_cont	2111	0.034	0.034	0.03 [-0.03, 0.10]	43.60	0.100	3.13E-01	0	0	0	0	CAB39L
19	13:49927732	rs9568188	t	c	0.7470	0.0247	DYSKINESIAS	DYSKINESIAS_surv	1856	0.062	0.067	1.06 [0.93, 1.21]	6.50	0.378	3.56E-01	0	0	0	0	CAB39L
20	13:49927732	rs9568188	t	c	0.7409	0.0284	UPDRS3_scaled	UPDRS3_scaled_cont	2446	-0.021	0.030	-0.02 [-0.08, 0.04]	0.00	0.866	4.78E-01	0	0	0	0	CAB39L
21	13:49927732	rs9568188	t	c	0.7556	0.0077	MOCA	MOCA_cont	1074	-0.100	0.141	-0.10 [-0.38, 0.18]	0.00	0.802	4.79E-01	0	0	0	0	CAB39L
22	13:49927732	rs9568188	t	c	0.7410	0.0251	CONST	CONST_base	1472	-0.062	0.097	0.94 [0.78, 1.14]	0.00	0.512	5.21E-01	0	0	0	0	CAB39L
23	13:49927732	rs9568188	t	c	0.7431	0.0210	MOTORFLUX	MOTORFLUX_base	1803	0.058	0.096	1.06 [0.88, 1.28]	26.10	0.247	5.46E-01	0	0	0	0	CAB39L
24	13:49927732	rs9568188	t	c	0.7355	0.0278	HYPOSOMIA	HYPOSOMIA_base	1588	-0.052	0.092	0.95 [0.79, 1.14]	0.00	0.651	5.70E-01	0	0	0	0	CAB39L
25	13:49927732	rs9568188	t	c	0.7298	0.0275	HY3	HY3_surv	2582	-0.038	0.072	0.96 [0.84, 1.11]	5.00	0.394	5.94E-01	0	0	0	0	CAB39L
26	13:49927732	rs9568188	t	c	0.7420	0.0174	MOTORFLUX	MOTORFLUX_surv	1709	-0.028	0.055	0.97 [0.87, 1.08]	0.00	0.969	6.13E-01	0	0	0	0	CAB39L
27	13:49927732	rs9568188	t	c	0.7438	0.0237	UPDRS2_scaled	UPDRS2_scaled_cont	2994	-0.012	0.027	-0.01 [-0.07, 0.04]	5.70	0.389	6.47E-01	0	0	0	0	CAB39L
28	13:49927732	rs9568188	t	c	0.7404	0.0276	HY	HY_cont	3627	-0.003	0.010	-0.00 [-0.02, 0.02]	40.00	0.074	7.32E-01	0	0	0	0	CAB39L
29	13:49927732	rs9568188	t	c	0.7369	0.0294	SLEEP	SLEEP_base	1724	0.025	0.095	1.03 [0.85, 1.23]	0.00	0.611	7.92E-01	0	0	0	0	CAB39L
30	13:49927732	rs9568188	t	c	0.7347	0.0206	COGi	COGi_base	2859	-0.019	0.098	0.98 [0.81, 1.19]	0.00	0.816	8.48E-01	0	0	0	0	CAB39L
31	13:49927732	rs9568188	t	c	0.7313	0.0253	HY3	HY3_base	1289	0.019	0.132	1.02 [0.79, 1.32]	0.00	0.581	8.86E-01	0	0	0	0	CAB39L
32	13:49927732	rs9568188	t	c	0.7472	0.0222	INS	INS_surv	1112	0.011	0.077	1.01 [0.87, 1.18]	0.00	0.426	8.91E-01	0	0	0	0	CAB39L
33	13:49927732	rs9568188	t	c	0.7496	0.0158	SEADL	SEADL_cont	2218	0.014	0.273	0.01 [-0.52, 0.55]	0.00	0.855	9.60E-01	0	0	0	0	CAB39L
34	13:49927732	rs9568188	t	c	0.7475	0.0204	DEPR	DEPR_surv	1314	-0.003	0.088	1.00 [0.84, 1.19]	0.00	0.759	9.76E-01	0	0	0	0	CAB39L
35	13:49927732	rs9568188	t	c	0.7417	0.0255	INS	INS_base	2220	-0.001	0.082	1.00 [0.85, 1.17]	36.60	0.137	9.93E-01	0	0	0	0	CAB39L
36	3:48748989	rs12497850	t	g	0.6440	0.0143	INS	INS_surv	1112	-0.175	0.067	0.84 [0.74, 0.96]	6.30	0.376	9.44E-03	0	0	0	0	IP6K2
37	3:48748989	rs12497850	t	g	0.6408	0.0134	MOCA	MOCA_cont	1074	0.237	0.123	0.24 [-0.01, 0.48]	0.00	0.447	5.51E-02	0	0	0	0	IP6K2
38	3:48748989	rs12497850	t	g	0.6399	0.0174	HY3	HY3_base	1289	0.182	0.121	1.20 [0.95, 1.52]	2.60	0.358	1.32E-01	0	0	0	0	IP6K2
39	3:48748989	rs12497850	t	g	0.6598	0.0174	UPDRS4_scaled	UPDRS4_scaled_cont	1798	0.034	0.026	0.03 [-0.02, 0.09]	0.00	0.497	2.03E-01	0	0	0	0	IP6K2
40	3:48748989	rs12497850	t	g	0.6550	0.0195	UPDRS1_scaled	UPDRS1_scaled_cont	2111	0.034	0.030	0.03 [-0.02, 0.09]	27.20	0.221	2.58E-01	0	0	0	0	IP6K2
41	3:48748989	rs12497850	t	g	0.6495	0.0239	HYPOSOMIA	HYPOSOMIA_base	1588	-0.088	0.084	0.92 [0.78, 1.08]	0.00	0.754	2.92E-01	0	0	0	0	IP6K2
42	3:48748989	rs12497850	t	g	0.6446	0.0235	COGi	COGi_base	2859	-0.093	0.090	0.91 [0.76, 1.09]	0.00	0.667	2.99E-01	0	0	0	0	IP6K2
43	3:48748989	rs12497850	t	g	0.6423	0.0119	DYSKINESIAS	DYSKINESIAS_surv	1856	0.048	0.059	1.05 [0.93, 1.18]	0.00	0.491	4.16E-01	0	0	0	0	IP6K2
44	3:48748989	rs12497850	t	g	0.6270	0.0271	HY3	HY3_surv	2582	-0.047	0.063	0.95 [0.84, 1.08]	0.00	0.914	4.58E-01	0	0	0	0	IP6K2
45	3:48748989	rs12497850	t	g	0.6444	0.0226	HY	HY_cont	3627	0.006	0.009	0.01 [-0.01, 0.02]	12.80	0.320	5.08E-01	0	0	0	0	IP6K2
46	3:48748989	rs12497850	t	g	0.6488	0.0164	DYSKINESIAS	DYSKINESIAS_base	1232	-0.069	0.105	0.93 [0.76, 1.15]	0.00	0.797	5.11E-01	0	0	0	0	IP6K2
47	3:48748989	rs12497850	t	g	0.6316	0.0147	DEPR	DEPR_surv	1314	-0.048	0.078	0.95 [0.82, 1.11]	0.00	0.857	5.38E-01	0	0	0	0	IP6K2
48	3:48748989	rs12497850	t	g	0.6438	0.0212	SLEEP	SLEEP_base	1724	0.047	0.086	1.05 [0.89, 1.24]	0.00	0.920	5.88E-01	0	0	0	0	IP6K2
49	3:48748989	rs12497850	t	g	0.6470	0.0239	UPDRS_scaled	UPDRS_scaled_cont	2994	0.012	0.024	0.01 [-0.04, 0.06]	0.00	0.813	6.34E-01	0	0	0	0	IP6K2
50	3:48748989	rs12497850	t	g	0.6508	0.0191	SEADL	SEADL_cont	2218	0.094	0.239	0.09 [-0.38, 0.56]	0.00	0.492	6.94E-01	0	0	0	0	IP6K2
51	3:48748989	rs12497850	t	g	0.6386	0.0153	DEPR	DEPR_base	2138	-0.030	0.092	0.97 [0.81, 1.16]	0.00	0.523	7.48E-01	0	0	0	0	IP6K2
52	3:48748989	rs12497850	t	g	0.6453	0.0210	MMSE	MMSE_cont	2114	0.010	0.045	0.01 [-0.08, 0.10]	19.70	0.274	8.22E-01	0	0	0	0	IP6K2
53	3:48748989	rs12497850	t	g	0.6563	0.0197	UPDRS2_scaled	UPDRS2_scaled_cont	2103	-0.005	0.030	-0.01 [-0.06, 0.05]	6.10	0.381	8.64E-01	0	0	0	0	IP6K2
54	3:48748989	rs12497850	t	g	0.6414	0.0149	CONST	CONST_base	1472	-0.015	0.088	0.99 [0.83, 1.17]	28.90	0.229	8.68E-01	0	0	0	0	IP6K2
55	3:48748989	rs12497850	t	g	0.6494	0.0147	MOTORFLUX	MOTORFLUX_base	1803	-0.014	0.085	0.99 [0.84, 1.16]	0.00	0.715	8.69E-01	0	0	0	0	IP6K2
56	3:48748989	rs12497850	t	g	0.6416	0.0205	MOTORFLUX	MOTORFLUX_surv	1709	0.003	0.050	1.00 [0.91, 1.11]	0.00	0.521	9.49E-01	0	0	0	0	IP6K2
57	3:48748989	rs12497850	t	g	0.6538	0.0188	UPDRS3_scaled	UPDRS3_scaled_cont	2446	0.001	0.027	0.00 [-0.05, 0.05]	0.00	0.928	9.75E-01	0	0	0	0	IP6K2
58	3:48748989	rs12497850	t	g	0.6511	0.0226	INS	INS_base	2220	-0.002	0.073	1.00 [0.86, 1.15]	0.00	0.671	9.77E-01	0	0	0	0	IP6K2
59	3:48748989	rs12497850	t	g	0.6506	0.0118	SEADL70	SEADL70_surv	1683	0.000	0.094	1.00 [0.83, 1.20]	0.00	0.632	9.97E-01	0	0	0	0	IP6K2
60	7:23300049	rs199351	a	c	0.6076	0.0192	DEPR	DEPR_base	2138	-0.242	0.093	0.79 [0.65, 0.94]	8.60	0.364	9.65E-03	0	0	0	0	GNPMB
61	7:23300049	rs199351	a	c	0.6086</															

1	17:44866805	rs11658976	a	g	0.5919	0.0241	INS	INS_base	2220	0.090	0.070	1.09 [0.95, 1.26]	0.00	0.440	2.03E-01	0	0	0	0	WNT3
2	17:44866805	rs11658976	a	g	0.5925	0.0279	HYPOSOMIA	HYPOSOMIA_base	1588	-0.096	0.080	0.91 [0.78, 1.06]	29.20	0.216	2.27E-01	0	0	0	0	WNT3
3	17:44866805	rs11658976	a	g	0.5801	0.0182	UPDRS1_scaled	UPDRS1_scaled_cont	2111	0.038	0.033	0.04 [-0.03, 0.10]	0.00	0.662	2.47E-01	0	0	0	0	WNT3
4	17:44866805	rs11658976	a	g	0.5973	0.0168	DEPR	DEPR_base	2138	0.092	0.089	1.10 [0.92, 1.31]	0.00	0.619	3.03E-01	0	0	0	0	WNT3
5	17:44866805	rs11658976	a	g	0.6053	0.0223	HY3	HY3_base	1289	-0.112	0.115	0.89 [0.71, 1.12]	63.50	0.064	3.29E-01	0	0	0	0	WNT3
6	17:44866805	rs11658976	a	g	0.5946	0.0245	COGI	COGI_base	2859	-0.071	0.085	0.93 [0.79, 1.10]	0.00	0.701	4.02E-01	0	0	0	0	WNT3
7	17:44866805	rs11658976	a	g	0.5789	0.0186	UPDRS2_scaled	UPDRS2_scaled_cont	2103	0.027	0.033	0.03 [-0.04, 0.09]	0.00	0.833	4.17E-01	0	0	0	0	WNT3
8	17:44866805	rs11658976	a	g	0.5917	0.0093	SEADL70	SEADL70_surv	1683	0.074	0.101	1.08 [0.88, 1.31]	0.00	0.612	4.63E-01	0	0	0	0	WNT3
9	17:44866805	rs11658976	a	g	0.5905	0.0036	MOCA	MOCA_cont	1074	-0.090	0.133	-0.09 [-0.35, 0.17]	0.00	0.968	4.96E-01	0	0	0	0	WNT3
10	17:44866805	rs11658976	a	g	0.5769	0.0208	MMSE	MMSE_cont	2114	0.030	0.048	0.03 [-0.06, 0.12]	0.00	0.718	5.33E-01	0	0	0	0	WNT3
11	17:44866805	rs11658976	a	g	0.6036	0.0322	HY3	HY3_surv	2582	0.041	0.069	1.04 [0.91, 1.19]	11.20	0.342	5.53E-01	0	0	0	0	WNT3
12	17:44866805	rs11658976	a	g	0.5794	0.0185	SEADL	SEADL_cont	2218	-0.146	0.256	-0.15 [-0.65, 0.35]	0.00	0.810	5.67E-01	0	0	0	0	WNT3
13	17:44866805	rs11658976	a	g	0.5949	0.0258	SLEEP	SLEEP_base	1724	-0.044	0.081	0.96 [0.82, 1.12]	0.00	0.777	5.86E-01	0	0	0	0	WNT3
14	17:44866805	rs11658976	a	g	0.5923	0.0250	COGI	COGI_surv	2244	-0.039	0.080	0.96 [0.82, 1.12]	0.00	0.604	6.28E-01	0	0	0	0	WNT3
15	17:44866805	rs11658976	a	g	0.5820	0.0209	UPDRS_scaled	UPDRS_scaled_cont	2994	0.012	0.026	0.01 [-0.04, 0.06]	0.00	0.905	6.48E-01	0	0	0	0	WNT3
16	17:44866805	rs11658976	a	g	0.5970	0.0172	DYSKINESIAS	DYSKINESIAS_surv	1856	0.030	0.067	1.03 [0.90, 1.17]	28.60	0.210	6.53E-01	0	0	0	0	WNT3
17	17:44866805	rs11658976	a	g	0.5869	0.0217	HY	HY_cont	3627	0.003	0.010	0.00 [-0.02, 0.02]	18.70	0.260	7.26E-01	0	0	0	0	WNT3
18	17:44866805	rs11658976	a	g	0.5924	0.0152	MOTORFLUX	MOTORFLUX_surv	1709	-0.017	0.055	0.98 [0.88, 1.09]	32.70	0.179	7.51E-01	0	0	0	0	WNT3
19	17:44866805	rs11658976	a	g	0.6017	0.0288	DEPR	DEPR_surv	1314	0.013	0.089	1.01 [0.85, 1.21]	0.00	0.737	8.85E-01	0	0	0	0	WNT3
20	17:44866805	rs11658976	a	g	0.5807	0.0171	UPDRS3_scaled	UPDRS3_scaled_cont	2446	-0.001	0.029	-0.00 [-0.06, 0.06]	0.00	0.927	9.74E-01	0	0	0	0	WNT3
21	17:44866805	rs11658976	a	g	0.5993	0.0192	CONST	CONST_base	1472	0.002	0.084	1.00 [0.85, 1.18]	1.80	0.396	9.85E-01	0	0	0	0	WNT3
22	3:28705690	rs6808178	t	c	0.3861	0.0201	MOCA	MOCA_cont	1074	-0.310	0.122	-0.31 [-0.55, -0.07]	0.00	0.639	1.07E-02	0	0	0	0	LINC00693
23	3:28705690	rs6808178	t	c	0.4039	0.0193	MOTORFLUX	MOTORFLUX_surv	1709	0.104	0.050	1.11 [1.01, 1.22]	0.00	0.841	3.94E-02	0	0	0	0	LINC00693
24	3:28705690	rs6808178	t	c	0.3909	0.0185	COGI	COGI_base	2859	0.167	0.089	1.18 [0.99, 1.41]	16.30	0.302	6.12E-02	0	0	0	0	LINC00693
25	3:28705690	rs6808178	t	c	0.3965	0.0116	MOTORFLUX	MOTORFLUX_base	1803	-0.123	0.085	0.88 [0.75, 1.04]	0.00	0.184	1.48E-01	0	0	0	0	LINC00693
26	3:28705690	rs6808178	t	c	0.3961	0.0178	SLEEP	SLEEP_base	1724	-0.125	0.087	0.88 [0.74, 1.05]	0.00	0.530	1.51E-01	0	0	0	0	LINC00693
27	3:28705690	rs6808178	t	c	0.3929	0.0153	SEADL	SEADL_cont	2218	-0.303	0.240	-0.30 [-0.77, 0.17]	0.00	0.849	2.06E-01	0	0	0	0	LINC00693
28	3:28705690	rs6808178	t	c	0.4036	0.0116	MMSE	MMSE_cont	2114	-0.052	0.046	-0.05 [-0.14, 0.04]	0.00	0.858	2.54E-01	0	0	0	0	LINC00693
29	3:28705690	rs6808178	t	c	0.4169	0.0099	DEPR	DEPR_surv	1314	-0.090	0.079	0.91 [0.78, 1.07]	0.00	0.731	2.55E-01	0	0	0	0	LINC00693
30	3:28705690	rs6808178	t	c	0.3948	0.0122	DYSKINESIAS	DYSKINESIAS_base	1232	0.119	0.106	1.13 [0.92, 1.38]	47.90	0.147	2.60E-01	0	0	0	0	LINC00693
31	3:28705690	rs6808178	t	c	0.4008	0.0119	DEPR	DEPR_base	2138	-0.093	0.093	0.91 [0.76, 1.09]	0.00	0.557	3.16E-01	0	0	0	0	LINC00693
32	3:28705690	rs6808178	t	c	0.3929	0.0186	HYPOSOMIA	HYPOSOMIA_base	1588	0.083	0.083	1.09 [0.92, 1.28]	1.60	0.406	3.20E-01	0	0	0	0	LINC00693
33	3:28705690	rs6808178	t	c	0.3977	0.0209	COGI	COGI_surv	2244	0.077	0.078	1.08 [0.93, 1.26]	31.90	0.163	3.21E-01	0	0	0	0	LINC00693
34	3:28705690	rs6808178	t	c	0.3974	0.0194	HY	HY_cont	3627	0.008	0.009	0.01 [-0.01, 0.03]	36.00	0.103	3.64E-01	0	0	0	0	LINC00693
35	3:28705690	rs6808178	t	c	0.3899	0.0107	SEADL70	SEADL70_surv	1683	0.069	0.093	1.07 [0.89, 1.29]	7.30	0.365	4.61E-01	0	0	0	0	LINC00693
36	3:28705690	rs6808178	t	c	0.4005	0.0163	HY3	HY3_base	1289	0.078	0.120	1.08 [0.85, 1.37]	32.90	0.225	5.19E-01	0	0	0	0	LINC00693
37	3:28705690	rs6808178	t	c	0.4041	0.0113	UPDRS1_scaled	UPDRS1_scaled_cont	2111	-0.017	0.030	-0.02 [-0.08, 0.04]	24.20	0.245	5.67E-01	0	0	0	0	LINC00693
38	3:28705690	rs6808178	t	c	0.3946	0.0161	INS	INS_base	2220	0.040	0.073	1.04 [0.90, 1.20]	35.40	0.146	5.85E-01	0	0	0	0	LINC00693
39	3:28705690	rs6808178	t	c	0.4124	0.0237	HY3	HY3_surv	2582	-0.035	0.065	0.97 [0.85, 1.10]	0.00	0.773	5.87E-01	0	0	0	0	LINC00693
40	3:28705690	rs6808178	t	c	0.3985	0.0173	UPDRS_scaled	UPDRS_scaled_cont	2994	0.013	0.024	0.01 [-0.03, 0.06]	0.00	0.726	5.87E-01	0	0	0	0	LINC00693
41	3:28705690	rs6808178	t	c	0.3924	0.0189	CONST	CONST_base	1472	0.042	0.087	1.04 [0.88, 1.24]	0.00	0.412	6.31E-01	0	0	0	0	LINC00693
42	3:28705690	rs6808178	t	c	0.4046	0.0113	UPDRS2_scaled	UPDRS2_scaled_cont	2103	0.009	0.030	0.01 [-0.05, 0.07]	0.00	0.518	7.75E-01	0	0	0	0	LINC00693
43	3:28705690	rs6808178	t	c	0.4111	0.0211	UPDRS3_scaled	UPDRS3_scaled_cont	2446	0.006	0.027	0.01 [-0.05, 0.06]	36.30	0.139	8.35E-01	0	0	0	0	LINC00693
44	3:28705690	rs6808178	t	c	0.3954	0.0199	INS	INS_surv	1112	0.010	0.068	1.01 [0.88, 1.15]	41.00	0.132	8.88E-01	0	0	0	0	LINC00693
45	3:28705690	rs6808178	t	c	0.4000	0.0163	DYSKINESIAS	DYSKINESIAS_surv	1856	-0.006	0.061	0.99 [0.88, 1.12]	0.00	0.449	9.26E-01	0	0	0	0	LINC00693
46	5:102365794	rs26431	c	g	0.7096	0.0138	DYSKINESIAS	DYSKINESIAS_base	1232	0.287	0.113	1.33 [1.07, 1.66]	0.00	0.685	1.10E-02	0	0	0	0	PAM
47	5:102365794	rs26431	c	g	0.7120	0.0183	INS	INS_base	2220	-0.138	0.075	0.87 [0.75, 1.01]	2.70	0.409	6.80E-02	0	0	0	0	PAM
48	5:102365794	rs26431	c	g	0.7123	0.0211	HYPOSOMIA	HYPOSOMIA_base	1588	0.112	0.087	1.12 [0.94, 1.33]	15.60	0.314	1.99E-01	0	0	0	0	PAM
49	5:102365794	rs26431	c	g	0.7112	0.0160	HY3	HY3_base	1289	-0.150	0.122	0.86 [0.68, 1.09]	0.00	0.894	2.20E-01	0	0	0	0	PAM
50	5:102365794	rs26431	c	g	0.7154	0.0191	MOTORFLUX	MOTORFLUX_base	1803	0.096	0.089	1.10 [0.93, 1.31]	0.00	0.599	2.80E-01	0	0	0	0	PAM
51	5:102365794	rs26431	c	g	0.7088	0.0204	SLEEP	SLEEP_base	1724	0.093	0.090	1.10 [0.92, 1.31]	41.80	0.112	3.01E-01	0	0	0	0	PAM
52	5:102365794	rs26431	c	g	0.7244	0.0205	SEADL	SEADL_cont	2218	0.254	0.263	0.25 [-0.26, 0.77]	0.00	0.467	3.34E-01	0	0	0	0	PAM
53	5:102365794	rs26431	c	g	0.7131	0.0216	UPDRS1_scaled	UPDRS1_scaled_cont	2111	0.026	0.032	0.03 [-0.04, 0.09]	4.40	0.393	4.18E-01	0	0	0	0	PAM
54	5:102365794	rs26431	c	g	0.7087	0.0182	DEPR	DEPR_surv	1314	0.064	0.088	1.07 [0.90, 1.27]	1.50	0.407	4.65E-01	0	0	0	0	PAM
55	5:102365794	rs26431	c	g	0.7130	0.0162	HY3	HY3_surv	2582	-0.047	0.067	0.95 [0.84, 1.09]	0.00	0.530	4.88E-01	0	0	0	0	PAM
56	5:102365794	rs26431	c	g	0.7115	0.0186	DEPR	DEPR_base	2138	0.068	0.099	1.07 [0.88, 1.30]	0.00	0.461	4.89E-01	0	0	0	0	PAM
57	5:102365794	rs26431	c	g	0.7128	0.0210	UPDRS3_scaled	UPDRS3_scaled_cont	2446	-0.017	0.028	-0.02 [-0.07, 0.04]	0.00	0.599	5.50E-01	0	0	0	0	PAM
58	5:102365794	rs26431	c	g	0.7088	0.0155	CONST	CONST_base	1472	0.052	0.091	1.05 [0.88, 1.26]	49.30	0.096	5.69E-01	0	0	0	0	PAM
59	5:102365794	rs26431	c	g	0.7114	0.0219	UPDRS2_scaled	UPDRS2_scaled_cont	2103	0.018	0.032	0.02 [-0.04, 0.08]	7.40	0.372	5.79E-01	0	0	0	0	PAM
60	5:102365794	rs26431	c	g	0.7096	0.0198	UPDRS_scaled	UPDRS_scaled_cont	2994	-0.014	0.026	-0.01 [-0.06, 0.04]	0.00	0.842	5.81E-01	0	0	0	0	PAM
61	5:102365794	rs26431	c	g	0.7130	0														

1	2:135464616	rs57891859	a	g	0.7270	0.0188	SLEEP	SLEEP_base	1724	-0.023	0.096	0.98 [0.81, 1.18]	0.00	0.506	8.13E-01	0	0	0	0	TMEM163
2	2:135464616	rs57891859	a	g	0.7349	0.0119	HY3	HY3_base	1289	0.032	0.141	1.03 [0.78, 1.36]	62.70	0.068	8.19E-01	0	0	0	0	TMEM163
2	2:135464616	rs57891859	a	g	0.7207	0.0164	INS	INS_surv	1112	0.015	0.071	1.02 [0.88, 1.17]	0.00	0.861	8.31E-01	0	0	0	0	TMEM163
3	2:135464616	rs57891859	a	g	0.7353	0.0175	UPDRS3_scaled	UPDRS3_scaled_cont	2446	-0.004	0.030	-0.00 [-0.06, 0.05]	10.10	0.351	8.88E-01	0	0	0	0	TMEM163
3	2:135464616	rs57891859	a	g	0.7279	0.0103	MOTORFLUX	MOTORFLUX_base	1803	0.009	0.094	1.01 [0.84, 1.21]	0.00	0.454	9.22E-01	0	0	0	0	TMEM163
4	3:122196892	rs55961674	t	c	0.1708	0.0163	SLEEP	SLEEP_base	1724	0.267	0.107	1.31 [1.06, 1.61]	0.00	0.768	1.30E-02	0	0	0	0	KPNA1
3	3:122196892	rs55961674	t	c	0.1662	0.0156	COGI	COGI_base	2859	-0.185	0.118	0.83 [0.66, 1.05]	0.00	0.902	1.17E-01	0	0	0	0	KPNA1
5	3:122196892	rs55961674	t	c	0.1641	0.0184	HY3	HY3_surv	2582	0.129	0.087	1.14 [0.96, 1.35]	30.60	0.174	1.35E-01	0	0	0	0	KPNA1
3	3:122196892	rs55961674	t	c	0.1800	0.0101	MOCA	MOCA_cont	1074	-0.183	0.160	-0.18 [-0.50, 0.13]	47.50	0.126	2.54E-01	0	0	0	0	KPNA1
6	3:122196892	rs55961674	t	c	0.1774	0.0170	INS	INS_base	2220	0.082	0.091	1.09 [0.91, 1.30]	0.00	0.719	3.68E-01	0	0	0	0	KPNA1
3	3:122196892	rs55961674	t	c	0.1769	0.0173	DYSKINESIAS	DYSKINESIAS_base	1232	-0.120	0.135	0.89 [0.68, 1.16]	0.00	0.848	3.76E-01	0	0	0	0	KPNA1
7	3:122196892	rs55961674	t	c	0.1738	0.0201	UPDRS_scaled	UPDRS_scaled_cont	2994	-0.028	0.032	-0.03 [-0.09, 0.03]	0.00	0.536	3.81E-01	0	0	0	0	KPNA1
3	3:122196892	rs55961674	t	c	0.1814	0.0280	INS	INS_surv	1112	0.067	0.088	1.07 [0.90, 1.27]	0.00	0.841	4.46E-01	0	0	0	0	KPNA1
8	3:122196892	rs55961674	t	c	0.1718	0.0096	SEADL70	SEADL70_surv	1683	0.085	0.122	1.09 [0.86, 1.38]	4.80	0.379	4.87E-01	0	0	0	0	KPNA1
3	3:122196892	rs55961674	t	c	0.1862	0.0233	DEPR	DEPR_surv	1314	0.067	0.105	1.07 [0.87, 1.31]	0.00	0.784	5.23E-01	0	0	0	0	KPNA1
9	3:122196892	rs55961674	t	c	0.1778	0.0229	DYSKINESIAS	DYSKINESIAS_surv	1856	-0.050	0.079	0.95 [0.81, 1.11]	0.00	0.833	5.29E-01	0	0	0	0	KPNA1
3	3:122196892	rs55961674	t	c	0.1794	0.0158	MMSE	MMSE_cont	2114	0.036	0.058	0.04 [-0.08, 0.15]	0.00	0.860	5.36E-01	0	0	0	0	KPNA1
10	3:122196892	rs55961674	t	c	0.1706	0.0215	MOTORFLUX	MOTORFLUX_surv	1709	-0.041	0.068	0.96 [0.84, 1.10]	0.00	0.575	5.42E-01	0	0	0	0	KPNA1
3	3:122196892	rs55961674	t	c	0.1742	0.0148	COGI	COGI_surv	2244	0.059	0.098	1.06 [0.87, 1.29]	0.00	0.769	5.49E-01	0	0	0	0	KPNA1
11	3:122196892	rs55961674	t	c	0.1684	0.0161	HY3	HY3_base	1289	0.080	0.153	1.08 [0.80, 1.46]	0.00	0.560	6.04E-01	0	0	0	0	KPNA1
3	3:122196892	rs55961674	t	c	0.1711	0.0189	HYPOSIMIA	HYPOSIMIA_base	1588	-0.049	0.103	0.95 [0.78, 1.16]	0.00	0.556	6.32E-01	0	0	0	0	KPNA1
12	3:122196892	rs55961674	t	c	0.1741	0.0214	HY	HY_cont	3627	-0.005	0.012	-0.00 [-0.03, 0.02]	10.70	0.340	6.90E-01	0	0	0	0	KPNA1
3	3:122196892	rs55961674	t	c	0.1774	0.0185	SEADL	SEADL_cont	2218	0.110	0.311	0.11 [-0.50, 0.72]	0.00	0.815	7.23E-01	0	0	0	0	KPNA1
13	3:122196892	rs55961674	t	c	0.1746	0.0194	UPDRS3_scaled	UPDRS3_scaled_cont	2446	-0.011	0.035	-0.01 [-0.08, 0.06]	42.10	0.098	7.48E-01	0	0	0	0	KPNA1
3	3:122196892	rs55961674	t	c	0.1704	0.0141	CONST	CONST_base	1472	-0.022	0.111	0.98 [0.79, 1.21]	0.00	0.976	8.40E-01	0	0	0	0	KPNA1
14	3:122196892	rs55961674	t	c	0.1789	0.0193	UPDRS4_scaled	UPDRS4_scaled_cont	1798	-0.005	0.034	-0.00 [-0.07, 0.06]	0.00	0.842	8.91E-01	0	0	0	0	KPNA1
3	3:122196892	rs55961674	t	c	0.1802	0.0185	UPDRS2_scaled	UPDRS2_scaled_cont	2103	0.003	0.039	0.00 [-0.07, 0.08]	34.90	0.162	9.49E-01	0	0	0	0	KPNA1
15	3:122196892	rs55961674	t	c	0.1750	0.0171	MOTORFLUX	MOTORFLUX_base	1803	0.006	0.108	1.01 [0.81, 1.24]	4.40	0.381	9.53E-01	0	0	0	0	KPNA1
3	3:122196892	rs55961674	t	c	0.1813	0.0183	UPDRS1_scaled	UPDRS1_scaled_cont	2111	0.002	0.039	0.00 [-0.07, 0.08]	0.00	0.603	9.55E-01	0	0	0	0	KPNA1
16	10:121536327	rs117896735	a	g	0.0219	0.0050	COGI	COGI_base	2483	0.700	0.283	2.01 [1.16, 3.50]	0.00	0.435	1.32E-02	0	0	0	0	INPP5F
3	10:121536327	rs117896735	a	g	0.0234	0.0035	MOTORFLUX	MOTORFLUX_surv	1709	0.290	0.162	1.34 [0.97, 1.83]	48.40	0.071	7.39E-02	0	0	0	0	INPP5F
17	10:121536327	rs117896735	a	g	0.0264	0.0056	MOCA	MOCA_cont	1074	-0.500	0.415	-0.50 [-1.31, 0.31]	46.60	0.132	2.29E-01	0	0	0	0	INPP5F
3	10:121536327	rs117896735	a	g	0.0273	0.0087	UPDRS_scaled	UPDRS_scaled_cont	2994	0.094	0.082	0.09 [-0.07, 0.25]	0.00	0.487	2.47E-01	0	0	0	0	INPP5F
18	10:121536327	rs117896735	a	g	0.0275	0.0103	UPDRS1_scaled	UPDRS1_scaled_cont	2111	0.108	0.104	0.11 [-0.10, 0.31]	0.00	0.915	3.00E-01	0	0	0	0	INPP5F
3	10:121536327	rs117896735	a	g	0.0182	0.0018	DYSKINESIAS	DYSKINESIAS_base	1232	-0.346	0.356	0.71 [0.35, 1.42]	6.50	0.343	3.31E-01	0	0	0	0	INPP5F
19	10:121536327	rs117896735	a	g	0.0256	0.0070	DEPR	DEPR_base	2138	-0.307	0.351	0.74 [0.37, 1.46]	0.00	0.911	3.82E-01	0	0	0	0	INPP5F
3	10:121536327	rs117896735	a	g	0.0232	0.0073	SLEEP	SLEEP_base	1724	0.219	0.270	1.25 [0.73, 2.11]	0.00	0.860	4.17E-01	0	0	0	0	INPP5F
20	10:121536327	rs117896735	a	g	0.0209	0.0039	CONST	CONST_base	1472	0.239	0.296	1.27 [0.71, 2.27]	25.00	0.255	4.19E-01	0	0	0	0	INPP5F
3	10:121536327	rs117896735	a	g	0.0239	0.0037	INS	INS_surv	1112	-0.162	0.212	0.85 [0.56, 1.29]	0.00	0.662	4.44E-01	0	0	0	0	INPP5F
21	10:121536327	rs117896735	a	g	0.0276	0.0110	UPDRS4_scaled	UPDRS4_scaled_cont	1798	0.065	0.091	0.07 [-0.11, 0.24]	41.10	0.131	4.75E-01	0	0	0	0	INPP5F
3	10:121536327	rs117896735	a	g	0.0254	0.0036	SEADL	SEADL_cont	2112	-0.512	0.798	-0.51 [-2.08, 1.05]	0.00	0.732	5.22E-01	0	0	0	0	INPP5F
22	10:121536327	rs117896735	a	g	0.0233	0.0031	DYSKINESIAS	DYSKINESIAS_surv	1856	0.124	0.193	1.13 [0.77, 1.65]	0.00	0.601	5.23E-01	0	0	0	0	INPP5F
3	10:121536327	rs117896735	a	g	0.0292	0.0066	HY3	HY3_surv	2582	-0.118	0.196	0.89 [0.60, 1.31]	0.00	0.973	5.48E-01	0	0	0	0	INPP5F
23	10:121536327	rs117896735	a	g	0.0227	0.0068	HYPOSIMIA	HYPOSIMIA_base	1588	0.156	0.261	1.17 [0.70, 1.95]	16.50	0.307	5.50E-01	0	0	0	0	INPP5F
3	10:121536327	rs117896735	a	g	0.0286	0.0098	HY	HY_cont	3627	-0.017	0.029	-0.02 [-0.07, 0.04]	0.00	0.591	5.51E-01	0	0	0	0	INPP5F
24	10:121536327	rs117896735	a	g	0.0221	0.0066	INS	INS_base	2220	-0.127	0.236	0.88 [0.55, 1.40]	0.00	0.582	5.91E-01	0	0	0	0	INPP5F
3	10:121536327	rs117896735	a	g	0.0220	0.0044	SEADL70	SEADL70_surv	1683	0.134	0.324	1.14 [0.61, 2.16]	0.00	0.804	6.78E-01	0	0	0	0	INPP5F
25	10:121536327	rs117896735	a	g	0.0233	0.0039	COGI	COGI_surv	2075	0.113	0.273	1.12 [0.66, 1.91]	0.00	0.983	6.80E-01	0	0	0	0	INPP5F
3	10:121536327	rs117896735	a	g	0.0252	0.0044	DEPR	DEPR_surv	1314	-0.066	0.277	0.94 [0.54, 1.61]	0.00	0.964	8.11E-01	0	0	0	0	INPP5F
26	10:121536327	rs117896735	a	g	0.0182	0.0023	MOTORFLUX	MOTORFLUX_base	1803	-0.067	0.296	0.94 [0.52, 1.67]	0.00	0.884	8.21E-01	0	0	0	0	INPP5F
3	10:121536327	rs117896735	a	g	0.0277	0.0105	UPDRS2_scaled	UPDRS2_scaled_cont	2103	-0.016	0.104	-0.02 [-0.22, 0.19]	0.00	0.698	8.78E-01	0	0	0	0	INPP5F
27	10:121536327	rs117896735	a	g	0.0297	0.0101	UPDRS3_scaled	UPDRS3_scaled_cont	2446	-0.012	0.088	-0.01 [-0.18, 0.16]	0.00	0.713	8.97E-01	0	0	0	0	INPP5F
3	10:121536327	rs117896735	a	g	0.0289	0.0078	MMSE	MMSE_cont	2114	0.014	0.143	0.01 [-0.27, 0.29]	0.00	0.931	9.21E-01	0	0	0	0	INPP5F
28	13:97865021	rs4771268	t	c	0.2272	0.0185	UPDRS3_scaled	UPDRS3_scaled_cont	2446	-0.075	0.030	-0.07 [-0.13, -0.02]	0.00	0.486	1.34E-02	0	0	0	0	MBNL2
3	13:97865021	rs4771268	t	c	0.2390	0.0098	UPDRS4_scaled	UPDRS4_scaled_cont	1798	-0.051	0.029	-0.05 [-0.11, 0.00]	0.00	0.601	7.29E-02	0	0	0	0	MBNL2
29	13:97865021	rs4771268	t	c	0.2336	0.0133	DYSKINESIAS	DYSKINESIAS_surv	1856	-0.112	0.068	0.89 [0.78, 1.02]	0.00	0.831	1.02E-01	0	0	0	0	MBNL2
3	13:97865021	rs4771268	t	c	0.2284	0.0159	UPDRS_scaled	UPDRS_scaled_cont	2994	-0.044	0.027	-0.04 [-0.10, 0.01]	0.00	0.443	1.10E-01	0	0	0	0	MBNL2
30	13:97865021	rs4771268	t	c	0.2198	0.0142	MMSE	MMSE_cont	2114	0.079	0.051	0.08 [-0.02, 0.18]	0.00	0.912	1.25E-01	0	0	0	0	MBNL2
3	13:97865021	rs4771268	t	c	0.2258	0.0119	HY3	HY3_base	1289	-0.196	0.139	0.82 [0.63, 1.08]	29.30	0.243	1.60E-01	0	0	0	0	MBNL2
31	13:97865021	rs4771268	t	c	0.2305	0.0197	HY	HY_cont	3627	-0.014	0.010	-0.01 [-0.03, 0.01]	0.00	0.453	1.75E-01	0	0	0	0	MBNL2
3	13:97865021																			

1	4:90626111	rs356182	a	g	0.5804	0.0238	COGi	COGi_surv	2244	-0.051	0.075	0.95 [0.82, 1.10]	23.30	0.236	4.98E-01	0	0	0	0	SNCA
2	4:90626111	rs356182	a	g	0.5852	0.0172	UPDRS_scaled	UPDRS_scaled_cont	2994	0.015	0.024	0.02 [-0.03, 0.06]	0.00	0.914	5.22E-01	0	0	0	0	SNCA
3	4:90626111	rs356182	a	g	0.5853	0.0121	UPDRS4_scaled	UPDRS4_scaled_cont	1798	-0.016	0.025	-0.02 [-0.07, 0.03]	0.00	0.505	5.32E-01	0	0	0	0	SNCA
4	4:90626111	rs356182	a	g	0.5978	0.0155	CONST	CONST_base	1472	0.040	0.086	1.04 [0.88, 1.23]	24.50	0.258	6.39E-01	0	0	0	0	SNCA
5	4:90626111	rs356182	a	g	0.5740	0.0222	SEADL	SEADL_cont	2218	-0.086	0.235	-0.09 [-0.55, 0.37]	0.00	0.591	7.14E-01	0	0	0	0	SNCA
6	4:90626111	rs356182	a	g	0.6000	0.0184	SLEEP	SLEEP_base	1724	0.029	0.085	1.03 [0.87, 1.22]	0.00	0.596	7.32E-01	0	0	0	0	SNCA
7	4:90626111	rs356182	a	g	0.5778	0.0227	HY3	HY3_surv	2582	-0.019	0.064	0.98 [0.87, 1.11]	29.80	0.181	7.68E-01	0	0	0	0	SNCA
8	4:90626111	rs356182	a	g	0.5820	0.0176	HY	HY_cont	3627	0.002	0.009	0.00 [-0.02, 0.02]	0.00	0.890	8.06E-01	0	0	0	0	SNCA
9	4:90626111	rs356182	a	g	0.5879	0.0160	SEADL70	SEADL70_surv	1683	-0.022	0.093	0.98 [0.82, 1.17]	45.60	0.119	8.15E-01	0	0	0	0	SNCA
10	4:90626111	rs356182	a	g	0.5973	0.0195	HY3	HY3_base	1289	0.019	0.117	1.02 [0.81, 1.28]	0.00	0.840	8.69E-01	0	0	0	0	SNCA
11	4:90626111	rs356182	a	g	0.6055	0.0167	INS	INS_base	2220	-0.009	0.071	0.99 [0.86, 1.14]	0.00	0.604	8.95E-01	0	0	0	0	SNCA
12	4:15737348	rs4698412	a	g	0.5809	0.0264	MOCA	MOCA_cont	1074	-0.285	0.117	-0.28 [-0.51, -0.06]	0.00	0.527	1.45E-02	0	0	0	0	BST1
13	4:15737348	rs4698412	a	g	0.5705	0.0164	UPDRS2_scaled	UPDRS2_scaled_cont	2103	-0.040	0.029	-0.04 [-0.10, 0.02]	0.00	0.584	1.63E-01	0	0	0	0	BST1
14	4:15737348	rs4698412	a	g	0.5681	0.0263	COGi	COGi_surv	2244	0.101	0.074	1.11 [0.96, 1.28]	0.00	0.930	1.74E-01	0	0	0	0	BST1
15	4:15737348	rs4698412	a	g	0.5697	0.0153	UPDRS1_scaled	UPDRS1_scaled_cont	2111	-0.038	0.029	-0.04 [-0.09, 0.02]	0.00	0.761	1.81E-01	0	0	0	0	BST1
16	4:15737348	rs4698412	a	g	0.5643	0.0203	HY3	HY3_base	1289	-0.138	0.116	0.87 [0.69, 1.09]	10.50	0.327	2.33E-01	0	0	0	0	BST1
17	4:15737348	rs4698412	a	g	0.5601	0.0181	CONST	CONST_base	1472	-0.102	0.086	0.90 [0.76, 1.07]	0.00	0.548	2.36E-01	0	0	0	0	BST1
18	4:15737348	rs4698412	a	g	0.5583	0.0154	MOTORFLUX	MOTORFLUX_base	1803	-0.077	0.081	0.93 [0.79, 1.09]	12.50	0.334	3.46E-01	0	0	0	0	BST1
19	4:15737348	rs4698412	a	g	0.5817	0.0208	SEADL	SEADL_cont	2112	0.215	0.229	0.22 [-0.23, 0.66]	0.00	0.861	3.48E-01	0	0	0	0	BST1
20	4:15737348	rs4698412	a	g	0.5698	0.0159	UPDRS3_scaled	UPDRS3_scaled_cont	2446	-0.023	0.026	-0.02 [-0.07, 0.03]	0.00	0.809	3.68E-01	0	0	0	0	BST1
21	4:15737348	rs4698412	a	g	0.5571	0.0168	HYPOSMIA	HYPOSMIA_base	1588	-0.069	0.081	0.93 [0.80, 1.09]	41.70	0.128	3.94E-01	0	0	0	0	BST1
22	4:15737348	rs4698412	a	g	0.5600	0.0146	INS	INS_base	2220	0.055	0.071	1.06 [0.92, 1.21]	12.10	0.336	4.35E-01	0	0	0	0	BST1
23	4:15737348	rs4698412	a	g	0.5757	0.0150	HY3	HY3_surv	2582	-0.046	0.063	0.96 [0.84, 1.08]	0.00	0.471	4.71E-01	0	0	0	0	BST1
24	4:15737348	rs4698412	a	g	0.5600	0.0164	DYSKINESIAS	DYSKINESIAS_base	1232	-0.069	0.102	0.93 [0.76, 1.14]	0.00	0.381	5.01E-01	0	0	0	0	BST1
25	4:15737348	rs4698412	a	g	0.5677	0.0222	INS	INS_surv	1112	0.043	0.064	1.04 [0.92, 1.18]	0.00	0.732	5.02E-01	0	0	0	0	BST1
26	4:15737348	rs4698412	a	g	0.5798	0.0127	HY	HY_cont	3627	0.006	0.009	0.01 [-0.01, 0.02]	0.00	0.612	5.12E-01	0	0	0	0	BST1
27	4:15737348	rs4698412	a	g	0.5625	0.0153	SEADL70	SEADL70_surv	1683	-0.050	0.092	0.95 [0.79, 1.14]	0.00	0.938	5.85E-01	0	0	0	0	BST1
28	4:15737348	rs4698412	a	g	0.5822	0.0086	MMSE	MMSE_cont	2114	-0.020	0.044	-0.02 [-0.11, 0.07]	2.80	0.408	6.56E-01	0	0	0	0	BST1
29	4:15737348	rs4698412	a	g	0.5741	0.0193	DYSKINESIAS	DYSKINESIAS_surv	1856	0.025	0.057	1.03 [0.92, 1.15]	0.00	0.808	6.56E-01	0	0	0	0	BST1
30	4:15737348	rs4698412	a	g	0.5734	0.0153	UPDRS_scaled	UPDRS_scaled_cont	2994	-0.007	0.023	-0.01 [-0.05, 0.04]	27.20	0.194	7.78E-01	0	0	0	0	BST1
31	4:15737348	rs4698412	a	g	0.5588	0.0182	SLEEP	SLEEP_base	1724	0.021	0.085	1.02 [0.86, 1.21]	0.00	0.623	8.09E-01	0	0	0	0	BST1
32	4:15737348	rs4698412	a	g	0.5767	0.0272	DEPR	DEPR_surv	1314	-0.017	0.077	0.98 [0.84, 1.14]	44.10	0.111	8.24E-01	0	0	0	0	BST1
33	4:15737348	rs4698412	a	g	0.5648	0.0205	COGi	COGi_base	2859	-0.019	0.087	0.98 [0.83, 1.16]	0.00	0.441	8.25E-01	0	0	0	0	BST1
34	4:15737348	rs4698412	a	g	0.5659	0.0156	UPDRS4_scaled	UPDRS4_scaled_cont	1798	-0.002	0.025	-0.00 [-0.05, 0.05]	0.00	0.501	9.27E-01	0	0	0	0	BST1
35	4:15737348	rs4698412	a	g	0.5663	0.0173	DEPR	DEPR_base	2138	-0.003	0.091	1.00 [0.83, 1.19]	17.00	0.296	9.70E-01	0	0	0	0	BST1
36	17:42294337	rs2269906	a	c	0.6706	0.0216	SLEEP	SLEEP_base	1724	-0.217	0.089	0.80 [0.68, 0.96]	0.00	0.636	1.46E-02	0	0	0	0	UBTF
37	17:42294337	rs2269906	a	c	0.6617	0.0210	UPDRS1_scaled	UPDRS1_scaled_cont	2111	-0.086	0.036	-0.09 [-0.16, -0.02]	38.40	0.136	1.56E-02	0	0	0	0	UBTF
38	17:42294337	rs2269906	a	c	0.6672	0.0172	CONST	CONST_base	1472	-0.171	0.090	0.84 [0.71, 1.01]	0.00	0.473	5.74E-02	0	0	0	0	UBTF
39	17:42294337	rs2269906	a	c	0.6544	0.0228	SEADL	SEADL_cont	2218	0.514	0.271	0.51 [-0.02, 1.05]	24.50	0.234	5.76E-02	0	0	0	0	UBTF
40	17:42294337	rs2269906	a	c	0.6608	0.0213	UPDRS2_scaled	UPDRS2_scaled_cont	2103	-0.067	0.035	-0.07 [-0.14, 0.00]	0.00	0.779	6.03E-02	0	0	0	0	UBTF
41	17:42294337	rs2269906	a	c	0.6591	0.0200	INS	INS_surv	1112	-0.138	0.074	0.87 [0.75, 1.01]	10.90	0.346	6.28E-02	0	0	0	0	UBTF
42	17:42294337	rs2269906	a	c	0.6687	0.0215	DEPR	DEPR_base	2138	-0.172	0.095	0.84 [0.70, 1.01]	0.00	0.923	6.90E-02	0	0	0	0	UBTF
43	17:42294337	rs2269906	a	c	0.6720	0.0254	UPDRS_scaled	UPDRS_scaled_cont	2994	-0.049	0.028	-0.05 [-0.10, 0.01]	0.00	0.961	8.08E-02	0	0	0	0	UBTF
44	17:42294337	rs2269906	a	c	0.6662	0.0212	HYPOSMIA	HYPOSMIA_base	1588	0.129	0.085	1.14 [0.96, 1.35]	0.00	0.976	1.30E-01	0	0	0	0	UBTF
45	17:42294337	rs2269906	a	c	0.6562	0.0202	MOTORFLUX	MOTORFLUX_base	1803	-0.117	0.086	0.89 [0.75, 1.05]	4.00	0.384	1.76E-01	0	0	0	0	UBTF
46	17:42294337	rs2269906	a	c	0.6728	0.0268	HY	HY_cont	3627	-0.010	0.010	-0.01 [-0.03, 0.01]	0.00	0.963	3.27E-01	0	0	0	0	UBTF
47	17:42294337	rs2269906	a	c	0.6645	0.0223	MOTORFLUX	MOTORFLUX_surv	1709	-0.050	0.057	0.95 [0.85, 1.06]	0.00	0.949	3.81E-01	0	0	0	0	UBTF
48	17:42294337	rs2269906	a	c	0.6654	0.0246	HY3	HY3_base	1289	-0.099	0.122	0.91 [0.71, 1.15]	2.70	0.358	4.17E-01	0	0	0	0	UBTF
49	17:42294337	rs2269906	a	c	0.6533	0.0204	DYSKINESIAS	DYSKINESIAS_base	1232	-0.086	0.107	0.92 [0.74, 1.13]	36.30	0.208	4.22E-01	0	0	0	0	UBTF
50	17:42294337	rs2269906	a	c	0.6694	0.0191	MMSE	MMSE_cont	2114	-0.035	0.050	-0.03 [-0.13, 0.06]	30.80	0.182	4.85E-01	0	0	0	0	UBTF
51	17:42294337	rs2269906	a	c	0.6482	0.0291	MOCA	MOCA_cont	1074	-0.091	0.143	-0.09 [-0.37, 0.19]	0.00	0.590	5.25E-01	0	0	0	0	UBTF
52	17:42294337	rs2269906	a	c	0.6591	0.0244	INS	INS_base	2220	0.038	0.074	1.04 [0.90, 1.20]	0.00	0.577	6.12E-01	0	0	0	0	UBTF
53	17:42294337	rs2269906	a	c	0.6682	0.0247	COGi	COGi_base	2859	-0.047	0.093	0.95 [0.80, 1.15]	15.80	0.306	6.15E-01	0	0	0	0	UBTF
54	17:42294337	rs2269906	a	c	0.6731	0.0192	DEPR	DEPR_surv	1314	-0.044	0.092	0.96 [0.80, 1.15]	44.10	0.111	6.34E-01	0	0	0	0	UBTF
55	17:42294337	rs2269906	a	c	0.6623	0.0125	SEADL70	SEADL70_surv	1683	-0.042	0.108	0.96 [0.78, 1.18]	4.50	0.381	6.94E-01	0	0	0	0	UBTF
56	17:42294337	rs2269906	a	c	0.6758	0.0219	HY3	HY3_surv	2582	-0.025	0.069	0.98 [0.85, 1.12]	0.00	0.827	7.14E-01	0	0	0	0	UBTF
57	17:42294337	rs2269906	a	c	0.6605	0.0213	UPDRS4_scaled	UPDRS4_scaled_cont	1798	-0.011	0.031	-0.01 [-0.07, 0.05]	0.00	0.557	7.17E-01	0	0	0	0	UBTF
58	17:42294337	rs2269906	a	c	0.6628	0.0230	DYSKINESIAS	DYSKINESIAS_surv	1856	0.022	0.070	1.02 [0.89, 1.17]	25.30	0.236	7.52E-01	0	0	0	0	UBTF
59	17:42294337	rs2269906	a	c	0.6643	0.0172	COGi	COGi_surv	2244	-0.024	0.085	0.98 [0.83, 1.15]	0.00	0.464	7.75E-01	0	0	0	0	UBTF
60	17:42294337	rs2269906	a	c	0.6645	0.0204	UPDRS3_scaled	UPDRS3_scaled_cont	2446	-0.006	0.031	-0.01 [-0.07, 0.05]	0.00	0.878	8.52E-01	0	0	0	0	UBTF
61	3:182760073	rs10513789	t	g	0.8232	0.0099	HY	HY_cont	3627	-0.027	0.011	-0.03 [-0.05, -0.01]	0.00	0.644	1.48E-02	0	0			

1	17:76425480	rs666463	a	t	0.8331	0.0149	MMSE	MMSE_cont	2114	-0.116	0.060	-0.12 [-0.23, 0.00]	41.50	0.102	5.46E-02	0	0	0	0	DNAH17
2	17:76425480	rs666463	a	t	0.8227	0.0124	UPDRS4_scaled	UPDRS4_scaled_cont	1798	0.051	0.033	0.05 [-0.01, 0.12]	0.00	0.513	1.20E-01	0	0	0	0	DNAH17
3	17:76425480	rs666463	a	t	0.8346	0.0159	DEPR	DEPR_base	2138	-0.164	0.121	0.85 [0.67, 1.08]	40.90	0.106	1.75E-01	0	0	0	0	DNAH17
4	17:76425480	rs666463	a	t	0.8283	0.0088	MOTORFLUX	MOTORFLUX_base	1803	0.134	0.108	1.14 [0.93, 1.41]	0.00	0.617	2.12E-01	0	0	0	0	DNAH17
5	17:76425480	rs666463	a	t	0.8365	0.0139	INS	INS_surv	1112	0.098	0.087	1.10 [0.93, 1.31]	0.00	0.505	2.60E-01	0	0	0	0	DNAH17
6	17:76425480	rs666463	a	t	0.8272	0.0157	SEADL70	SEADL70_surv	1683	0.131	0.123	1.14 [0.90, 1.45]	43.00	0.135	2.86E-01	0	0	0	0	DNAH17
7	17:76425480	rs666463	a	t	0.8190	0.0210	HY3	HY3_surv	2582	-0.064	0.078	0.94 [0.81, 1.09]	0.00	0.665	4.14E-01	0	0	0	0	DNAH17
8	17:76425480	rs666463	a	t	0.8397	0.0278	DEPR	DEPR_surv	1314	0.088	0.109	1.09 [0.88, 1.35]	0.00	0.965	4.19E-01	0	0	0	0	DNAH17
9	17:76425480	rs666463	a	t	0.8310	0.0204	MOCA	MOCA_cont	1074	-0.114	0.164	-0.11 [-0.44, 0.21]	45.10	0.141	4.89E-01	0	0	0	0	DNAH17
10	17:76425480	rs666463	a	t	0.8258	0.0082	COGI	COGI_base	2859	0.072	0.111	1.07 [0.86, 1.34]	0.00	0.745	5.16E-01	0	0	0	0	DNAH17
11	17:76425480	rs666463	a	t	0.8289	0.0196	UPDRS1_scaled	UPDRS1_scaled_cont	2111	-0.025	0.039	-0.03 [-0.10, 0.05]	16.00	0.308	5.19E-01	0	0	0	0	DNAH17
12	17:76425480	rs666463	a	t	0.8247	0.0205	DYSKINESIAS	DYSKINESIAS_surv	1856	0.046	0.075	1.05 [0.90, 1.21]	0.00	0.847	5.38E-01	0	0	0	0	DNAH17
13	17:76425480	rs666463	a	t	0.8267	0.0173	COGI	COGI_surv	2244	0.050	0.097	1.05 [0.87, 1.27]	0.00	0.648	6.07E-01	0	0	0	0	DNAH17
14	17:76425480	rs666463	a	t	0.8272	0.0073	CONST	CONST_base	1472	0.036	0.109	1.04 [0.84, 1.28]	37.50	0.171	7.42E-01	0	0	0	0	DNAH17
15	17:76425480	rs666463	a	t	0.8256	0.0088	SLEEP	SLEEP_base	1724	-0.026	0.108	0.97 [0.79, 1.20]	0.00	0.864	8.07E-01	0	0	0	0	DNAH17
16	17:76425480	rs666463	a	t	0.8249	0.0090	HYPOSOMIA	HYPOSOMIA_base	1588	-0.022	0.102	0.98 [0.80, 1.19]	0.00	0.481	8.32E-01	0	0	0	0	DNAH17
17	17:76425480	rs666463	a	t	0.8269	0.0159	UPDRS3_scaled	UPDRS3_scaled_cont	2446	-0.003	0.035	-0.00 [-0.07, 0.06]	17.80	0.290	9.30E-01	0	0	0	0	DNAH17
18	17:42434630	rs850738	a	g	0.5920	0.0205	MMSE	MMSE_cont	2114	0.109	0.045	0.11 [0.02, 0.20]	44.30	0.083	1.67E-02	0	0	0	0	FAM171A2
19	17:42434630	rs850738	a	g	0.5854	0.0268	COGI	COGI_base	2859	-0.207	0.087	0.81 [0.69, 0.96]	0.00	0.905	1.72E-02	0	0	0	0	FAM171A2
20	17:42434630	rs850738	a	g	0.5964	0.0192	UPDRS_scaled	UPDRS_scaled_cont	2994	-0.050	0.024	-0.05 [-0.10, -0.00]	0.00	0.597	3.57E-02	0	0	0	0	FAM171A2
21	17:42434630	rs850738	a	g	0.5851	0.0279	DYSKINESIAS	DYSKINESIAS_base	1232	-0.215	0.104	0.81 [0.66, 0.99]	0.00	0.595	3.80E-02	0	0	0	0	FAM171A2
22	17:42434630	rs850738	a	g	0.5970	0.0148	UPDRS2_scaled	UPDRS2_scaled_cont	2103	-0.059	0.029	-0.06 [-0.12, -0.00]	0.00	0.578	4.63E-02	0	0	0	0	FAM171A2
23	17:42434630	rs850738	a	g	0.5976	0.0239	COGI	COGI_surv	2244	-0.132	0.077	0.88 [0.75, 1.02]	0.00	0.697	8.54E-02	0	0	0	0	FAM171A2
24	17:42434630	rs850738	a	g	0.5871	0.0255	MOTORFLUX	MOTORFLUX_base	1803	-0.128	0.082	0.88 [0.75, 1.03]	30.80	0.216	1.18E-01	0	0	0	0	FAM171A2
25	17:42434630	rs850738	a	g	0.5946	0.0170	UPDRS3_scaled	UPDRS3_scaled_cont	2446	-0.041	0.026	-0.04 [-0.09, 0.01]	0.00	0.663	1.20E-01	0	0	0	0	FAM171A2
26	17:42434630	rs850738	a	g	0.5908	0.0269	MOTORFLUX	MOTORFLUX_surv	1709	-0.074	0.050	0.93 [0.84, 1.02]	0.00	0.907	1.35E-01	0	0	0	0	FAM171A2
27	17:42434630	rs850738	a	g	0.5939	0.0261	DYSKINESIAS	DYSKINESIAS_surv	1856	-0.087	0.060	0.92 [0.82, 1.03]	0.00	0.938	1.44E-01	0	0	0	0	FAM171A2
28	17:42434630	rs850738	a	g	0.5866	0.0213	HY	HY_cont	3627	-0.012	0.009	-0.01 [-0.03, 0.01]	0.00	0.591	1.96E-01	0	0	0	0	FAM171A2
29	17:42434630	rs850738	a	g	0.5955	0.0144	UPDRS4_scaled	UPDRS4_scaled_cont	1798	-0.032	0.026	-0.03 [-0.08, 0.02]	0.00	0.689	2.12E-01	0	0	0	0	FAM171A2
30	17:42434630	rs850738	a	g	0.5965	0.0137	UPDRS1_scaled	UPDRS1_scaled_cont	2111	-0.034	0.030	-0.03 [-0.09, 0.02]	0.00	0.554	2.42E-01	0	0	0	0	FAM171A2
31	17:42434630	rs850738	a	g	0.5885	0.0290	HYPOSOMIA	HYPOSOMIA_base	1588	-0.094	0.082	0.91 [0.78, 1.07]	13.70	0.327	2.48E-01	0	0	0	0	FAM171A2
32	17:42434630	rs850738	a	g	0.5975	0.0130	SEADL	SEADL_cont	2218	0.252	0.240	0.25 [-0.22, 0.72]	2.30	0.412	2.94E-01	0	0	0	0	FAM171A2
33	17:42434630	rs850738	a	g	0.5869	0.0351	INS	INS_surv	1112	-0.058	0.066	0.94 [0.83, 1.08]	0.20	0.415	3.86E-01	0	0	0	0	FAM171A2
34	17:42434630	rs850738	a	g	0.5874	0.0321	CONST	CONST_base	1472	0.068	0.086	1.07 [0.90, 1.27]	0.00	0.448	4.33E-01	0	0	0	0	FAM171A2
35	17:42434630	rs850738	a	g	0.5697	0.0417	HY3	HY3_surv	2582	-0.045	0.066	0.96 [0.84, 1.09]	0.00	0.776	4.95E-01	0	0	0	0	FAM171A2
36	17:42434630	rs850738	a	g	0.6009	0.0225	MOCA	MOCA_cont	1074	-0.075	0.123	-0.07 [-0.32, 0.17]	0.00	0.821	5.45E-01	0	0	0	0	FAM171A2
37	17:42434630	rs850738	a	g	0.6032	0.0158	SEADL70	SEADL70_surv	1683	-0.051	0.096	0.95 [0.79, 1.15]	0.00	0.506	5.96E-01	0	0	0	0	FAM171A2
38	17:42434630	rs850738	a	g	0.5874	0.0381	DEPR	DEPR_surv	1314	-0.032	0.081	0.97 [0.83, 1.13]	41.30	0.130	6.91E-01	0	0	0	0	FAM171A2
39	17:42434630	rs850738	a	g	0.5904	0.0273	DEPR	DEPR_base	2138	-0.001	0.091	1.00 [0.84, 1.19]	27.90	0.205	9.92E-01	0	0	0	0	FAM171A2
40	490636630	rs519538	a	g	0.6699	0.0086	MOTORFLUX	MOTORFLUX_base	1803	-0.196	0.083	0.82 [0.70, 0.97]	46.30	0.114	1.80E-02	0	0	0	0	SNCA
41	490636630	rs519538	a	g	0.6691	0.0131	MOTORFLUX	MOTORFLUX_surv	1709	-0.114	0.051	0.89 [0.81, 0.98]	0.00	0.888	2.37E-02	0	0	0	0	SNCA
42	490636630	rs519538	a	g	0.6709	0.0097	DYSKINESIAS	DYSKINESIAS_base	1232	-0.229	0.103	0.80 [0.65, 0.97]	14.30	0.311	2.54E-02	0	0	0	0	SNCA
43	490636630	rs519538	a	g	0.6593	0.0095	DEPR	DEPR_surv	1314	0.169	0.082	1.18 [1.01, 1.39]	0.00	0.712	3.99E-02	0	0	0	0	SNCA
44	490636630	rs519538	a	g	0.6574	0.0110	UPDRS1_scaled	UPDRS1_scaled_cont	2111	0.058	0.030	0.06 [-0.00, 0.12]	0.00	0.875	5.52E-02	0	0	0	0	SNCA
45	490636630	rs519538	a	g	0.6674	0.0095	CONST	CONST_base	1472	0.142	0.088	1.15 [0.97, 1.37]	0.00	0.578	1.07E-01	0	0	0	0	SNCA
46	490636630	rs519538	a	g	0.6694	0.0138	DEPR	DEPR_base	2138	0.138	0.095	1.15 [0.95, 1.38]	0.00	0.954	1.45E-01	0	0	0	0	SNCA
47	490636630	rs519538	a	g	0.6659	0.0098	COGI	COGI_base	2859	0.114	0.090	1.12 [0.94, 1.34]	0.00	0.495	2.05E-01	0	0	0	0	SNCA
48	490636630	rs519538	a	g	0.6672	0.0088	DYSKINESIAS	DYSKINESIAS_surv	1856	-0.064	0.059	0.94 [0.84, 1.05]	0.00	0.854	2.82E-01	0	0	0	0	SNCA
49	490636630	rs519538	a	g	0.6587	0.0114	UPDRS4_scaled	UPDRS4_scaled_cont	1798	-0.023	0.026	-0.01 [-0.07, 0.03]	0.00	0.507	3.72E-01	0	0	0	0	SNCA
50	490636630	rs519538	a	g	0.6518	0.0190	MMSE	MMSE_cont	2114	-0.042	0.047	-0.04 [-0.13, 0.05]	0.00	0.544	3.73E-01	0	0	0	0	SNCA
51	490636630	rs519538	a	g	0.6564	0.0170	HY	HY_cont	3627	0.007	0.009	0.01 [-0.01, 0.03]	3.10	0.414	4.37E-01	0	0	0	0	SNCA
52	490636630	rs519538	a	g	0.6698	0.0129	SLEEP	SLEEP_base	1724	0.066	0.087	1.07 [0.90, 1.27]	0.00	0.636	4.53E-01	0	0	0	0	SNCA
53	490636630	rs519538	a	g	0.6570	0.0171	UPDRS_scaled	UPDRS_scaled_cont	2994	0.017	0.025	0.02 [-0.03, 0.07]	0.00	0.478	4.78E-01	0	0	0	0	SNCA
54	490636630	rs519538	a	g	0.6661	0.0092	HY3	HY3_base	1289	-0.076	0.117	0.93 [0.74, 1.17]	4.20	0.352	5.14E-01	0	0	0	0	SNCA
55	490636630	rs519538	a	g	0.6569	0.0106	UPDRS2_scaled	UPDRS2_scaled_cont	2103	0.017	0.030	0.02 [-0.04, 0.08]	0.00	0.469	5.62E-01	0	0	0	0	SNCA
56	490636630	rs519538	a	g	0.6417	0.0167	MOCA	MOCA_cont	1074	-0.066	0.124	-0.07 [-0.31, 0.18]	0.00	0.831	5.95E-01	0	0	0	0	SNCA
57	490636630	rs519538	a	g	0.6599	0.0135	SEADL70	SEADL70_surv	1683	0.044	0.097	1.04 [0.86, 1.26]	0.00	0.435	6.52E-01	0	0	0	0	SNCA
58	490636630	rs519538	a	g	0.6582	0.0175	COGI	COGI_surv	2244	0.027	0.078	1.03 [0.88, 1.20]	0.00	0.472	7.28E-01	0	0	0	0	SNCA
59	490636630	rs519538	a	g	0.6690	0.0105	HYPOSOMIA	HYPOSOMIA_base	1588	-0.027	0.084	0.97 [0.83, 1.15]	0.00	0.537	7.50E-01	0	0	0	0	SNCA
60	490636630	rs519538	a	g	0.6474	0.0196	SEADL	SEADL_cont	2218	-0.060	0.243	-0.06 [-0.54, 0.42]	0.00	0.629	8.07E-01	0	0	0	0	SNCA
61	490636630	rs519538	a	g	0.6640	0.0082	INS	INS_surv	1112	-0.016	0.067	0.98 [0.86, 1.12]	0.00							

1	9:17579690	rs13294100	t	g	0.3311	0.0151	CONST	CONST_base	1472	-0.152	0.089	0.86 [0.72, 1.02]	0.00	0.923	8.92E-02	0	0	0	0	SH3GL2
2	9:17579690	rs13294100	t	g	0.3424	0.0155	MOTORFLUX	MOTORFLUX_base	1803	-0.127	0.086	0.88 [0.74, 1.04]	0.00	0.637	1.40E-01	0	0	0	0	SH3GL2
3	9:17579690	rs13294100	t	g	0.3290	0.0218	DYSKINESIAS	DYSKINESIAS_surv	1856	-0.088	0.061	0.92 [0.81, 1.03]	0.00	0.729	1.52E-01	0	0	0	0	SH3GL2
4	9:17579690	rs13294100	t	g	0.3321	0.0199	HY3	HY3_base	1289	-0.172	0.123	0.84 [0.66, 1.07]	27.70	0.251	1.62E-01	0	0	0	0	SH3GL2
5	9:17579690	rs13294100	t	g	0.3319	0.0201	UPDRS4_scaled	UPDRS4_scaled_cont	1798	-0.033	0.026	-0.03 [-0.08, 0.02]	0.00	0.993	2.09E-01	0	0	0	0	SH3GL2
6	9:17579690	rs13294100	t	g	0.3322	0.0191	UPDRS2_scaled	UPDRS2_scaled_cont	2103	0.031	0.030	0.03 [-0.03, 0.09]	0.00	0.993	2.97E-01	0	0	0	0	SH3GL2
7	9:17579690	rs13294100	t	g	0.3349	0.0162	HYPOSIMIA	HYPOSIMIA_base	1588	-0.084	0.084	0.92 [0.78, 1.08]	0.00	0.895	3.15E-01	0	0	0	0	SH3GL2
8	9:17579690	rs13294100	t	g	0.3335	0.0102	MMSE	MMSE_cont	2114	0.045	0.046	0.04 [-0.05, 0.14]	33.60	0.160	3.30E-01	0	0	0	0	SH3GL2
9	9:17579690	rs13294100	t	g	0.3411	0.0150	SEADL	SEADL_cont	2218	0.222	0.247	0.22 [-0.26, 0.71]	0.00	0.777	3.69E-01	0	0	0	0	SH3GL2
10	9:17579690	rs13294100	t	g	0.3294	0.0172	COGI	COGI_surv	2244	0.041	0.079	1.04 [0.89, 1.22]	0.00	0.611	6.08E-01	0	0	0	0	SH3GL2
11	9:17579690	rs13294100	t	g	0.3249	0.0209	INS	INS_surv	1112	-0.035	0.070	0.97 [0.84, 1.11]	9.30	0.356	6.23E-01	0	0	0	0	SH3GL2
12	9:17579690	rs13294100	t	g	0.3393	0.0153	INS	INS_base	2220	0.032	0.074	1.03 [0.89, 1.19]	36.90	0.134	6.62E-01	0	0	0	0	SH3GL2
13	9:17579690	rs13294100	t	g	0.3254	0.0235	DEPR	DEPR_surv	1314	-0.034	0.084	0.97 [0.82, 1.14]	0.00	0.945	6.86E-01	0	0	0	0	SH3GL2
14	9:17579690	rs13294100	t	g	0.3357	0.0186	MOTORFLUX	MOTORFLUX_surv	1709	-0.019	0.053	0.98 [0.88, 1.09]	0.00	0.591	7.20E-01	0	0	0	0	SH3GL2
15	9:17579690	rs13294100	t	g	0.3339	0.0171	UPDRS_scaled	UPDRS_scaled_cont	2994	0.009	0.024	0.01 [-0.04, 0.06]	0.00	0.838	7.20E-01	0	0	0	0	SH3GL2
16	9:17579690	rs13294100	t	g	0.3407	0.0156	DEPR	DEPR_base	2138	0.026	0.092	1.03 [0.86, 1.23]	0.00	0.710	7.74E-01	0	0	0	0	SH3GL2
17	9:17579690	rs13294100	t	g	0.3348	0.0169	SLEEP	SLEEP_base	1724	-0.025	0.087	0.98 [0.82, 1.16]	33.90	0.169	7.78E-01	0	0	0	0	SH3GL2
18	9:17579690	rs13294100	t	g	0.3413	0.0161	DYSKINESIAS	DYSKINESIAS_base	1232	0.025	0.106	1.03 [0.83, 1.26]	0.00	0.372	8.14E-01	0	0	0	0	SH3GL2
19	9:17579690	rs13294100	t	g	0.3343	0.0188	UPDRS1_scaled	UPDRS1_scaled_cont	2111	-0.005	0.030	-0.01 [-0.06, 0.05]	0.00	0.972	8.65E-01	0	0	0	0	SH3GL2
20	9:17579690	rs13294100	t	g	0.3328	0.0232	SEADL70	SEADL70_surv	1683	-0.013	0.097	0.99 [0.82, 1.19]	0.00	0.552	8.94E-01	0	0	0	0	SH3GL2
21	9:17579690	rs13294100	t	g	0.3327	0.0179	UPDRS3_scaled	UPDRS3_scaled_cont	2446	0.004	0.027	0.00 [-0.05, 0.06]	0.00	0.672	8.97E-01	0	0	0	0	SH3GL2
22	4:77198054	rs6854006	t	c	0.3482	0.0132	HY3	HY3_base	1289	0.267	0.119	1.31 [1.03, 1.65]	25.70	0.261	2.55E-02	0	0	0	0	FAM47E-STBD1
23	4:77198054	rs6854006	t	c	0.3504	0.0110	DYSKINESIAS	DYSKINESIAS_base	1232	0.191	0.105	1.21 [0.98, 1.49]	60.60	0.079	7.03E-02	0	0	0	0	FAM47E-STBD1
24	4:77198054	rs6854006	t	c	0.3481	0.0247	SLEEP	SLEEP_base	1724	0.130	0.085	1.14 [0.96, 1.35]	0.00	0.831	1.27E-01	0	0	0	0	FAM47E-STBD1
25	4:77198054	rs6854006	t	c	0.3550	0.0212	HYPOSIMIA	HYPOSIMIA_base	1588	-0.106	0.082	0.90 [0.77, 1.06]	0.00	0.708	1.93E-01	0	0	0	0	FAM47E-STBD1
26	4:77198054	rs6854006	t	c	0.3354	0.0216	HY	HY_cont	3627	0.011	0.009	0.01 [-0.01, 0.03]	19.70	0.250	2.05E-01	0	0	0	0	FAM47E-STBD1
27	4:77198054	rs6854006	t	c	0.3370	0.0192	UPDRS2_scaled	UPDRS2_scaled_cont	2103	0.035	0.030	0.03 [-0.02, 0.09]	0.00	0.864	2.46E-01	0	0	0	0	FAM47E-STBD1
28	4:77198054	rs6854006	t	c	0.3370	0.0194	UPDRS4_scaled	UPDRS4_scaled_cont	1798	0.030	0.026	0.03 [-0.02, 0.08]	0.00	0.729	2.52E-01	0	0	0	0	FAM47E-STBD1
29	4:77198054	rs6854006	t	c	0.3484	0.0188	COGI	COGI_base	2859	0.096	0.087	1.10 [0.93, 1.30]	0.00	0.728	2.72E-01	0	0	0	0	FAM47E-STBD1
30	4:77198054	rs6854006	t	c	0.3472	0.0141	MOTORFLUX	MOTORFLUX_base	1803	-0.082	0.085	0.92 [0.78, 1.09]	0.00	0.694	3.34E-01	0	0	0	0	FAM47E-STBD1
31	4:77198054	rs6854006	t	c	0.3388	0.0202	DEPR	DEPR_base	2138	0.089	0.093	1.09 [0.91, 1.31]	0.00	0.716	3.39E-01	0	0	0	0	FAM47E-STBD1
32	4:77198054	rs6854006	t	c	0.3281	0.0179	MMSE	MMSE_cont	2114	-0.043	0.047	-0.04 [-0.13, 0.05]	0.00	0.588	3.60E-01	0	0	0	0	FAM47E-STBD1
33	4:77198054	rs6854006	t	c	0.3363	0.0189	UPDRS1_scaled	UPDRS1_scaled_cont	2111	0.025	0.030	0.02 [-0.03, 0.08]	0.00	0.980	4.09E-01	0	0	0	0	FAM47E-STBD1
34	4:77198054	rs6854006	t	c	0.3417	0.0211	INS	INS_surv	1112	-0.047	0.066	0.95 [0.84, 1.09]	0.00	0.549	4.79E-01	0	0	0	0	FAM47E-STBD1
35	4:77198054	rs6854006	t	c	0.3330	0.0050	DEPR	DEPR_surv	1314	0.054	0.080	1.06 [0.90, 1.23]	17.10	0.303	4.98E-01	0	0	0	0	FAM47E-STBD1
36	4:77198054	rs6854006	t	c	0.3398	0.0192	MOCA	MOCA_cont	1074	-0.078	0.120	-0.08 [-0.31, 0.16]	0.00	0.930	5.18E-01	0	0	0	0	FAM47E-STBD1
37	4:77198054	rs6854006	t	c	0.3319	0.0203	UPDRS_scaled	UPDRS_scaled_cont	2994	0.016	0.024	0.02 [-0.03, 0.06]	11.60	0.336	5.18E-01	0	0	0	0	FAM47E-STBD1
38	4:77198054	rs6854006	t	c	0.3484	0.0226	CONST	CONST_base	1472	-0.049	0.086	0.95 [0.80, 1.13]	0.00	0.895	5.74E-01	0	0	0	0	FAM47E-STBD1
39	4:77198054	rs6854006	t	c	0.3463	0.0130	MOTORFLUX	MOTORFLUX_surv	1709	0.022	0.050	1.02 [0.93, 1.13]	47.00	0.079	6.68E-01	0	0	0	0	FAM47E-STBD1
40	4:77198054	rs6854006	t	c	0.3376	0.0168	DYSKINESIAS	DYSKINESIAS_surv	1856	-0.022	0.061	0.98 [0.87, 1.10]	48.30	0.071	7.24E-01	0	0	0	0	FAM47E-STBD1
41	4:77198054	rs6854006	t	c	0.3418	0.0158	SEADL70	SEADL70_surv	1683	0.030	0.094	1.03 [0.86, 1.24]	0.00	0.488	7.54E-01	0	0	0	0	FAM47E-STBD1
42	4:77198054	rs6854006	t	c	0.3422	0.0183	SEADL	SEADL_cont	2218	-0.064	0.239	-0.06 [-0.53, 0.40]	0.00	0.628	7.88E-01	0	0	0	0	FAM47E-STBD1
43	4:77198054	rs6854006	t	c	0.3344	0.0275	COGI	COGI_surv	2244	-0.001	0.075	1.00 [0.86, 1.16]	0.00	0.831	9.89E-01	0	0	0	0	FAM47E-STBD1
44	2:96000943	rs2024277	a	t	0.2330	0.0219	COGI	COGI_surv	2244	0.208	0.094	1.23 [1.03, 1.48]	0.00	0.848	2.61E-02	0	0	0	0	KCNIP3
45	2:96000943	rs2024277	a	t	0.2217	0.0206	SLEEP	SLEEP_base	1724	0.163	0.099	1.18 [0.97, 1.43]	0.00	0.834	9.80E-02	0	0	0	0	KCNIP3
46	2:96000943	rs2024277	a	t	0.2291	0.0172	INS	INS_surv	1112	-0.142	0.087	0.87 [0.73, 1.03]	0.00	0.510	1.03E-01	0	0	0	0	KCNIP3
47	2:96000943	rs2024277	a	t	0.2323	0.0234	DEPR	DEPR_base	2138	0.163	0.105	1.18 [0.96, 1.45]	0.00	0.705	1.20E-01	0	0	0	0	KCNIP3
48	2:96000943	rs2024277	a	t	0.2398	0.0121	SEADL70	SEADL70_surv	1683	-0.170	0.127	0.84 [0.66, 1.08]	14.50	0.322	1.81E-01	0	0	0	0	KCNIP3
49	2:96000943	rs2024277	a	t	0.2340	0.0180	MOTORFLUX	MOTORFLUX_base	1803	0.131	0.098	1.14 [0.94, 1.38]	0.00	0.635	1.82E-01	0	0	0	0	KCNIP3
50	2:96000943	rs2024277	a	t	0.2308	0.0124	HY3	HY3_surv	2582	0.093	0.076	1.10 [0.95, 1.27]	0.00	0.982	2.22E-01	0	0	0	0	KCNIP3
51	2:96000943	rs2024277	a	t	0.2385	0.0195	MOCA	MOCA_cont	1074	0.179	0.161	1.18 [-0.14, 0.50]	0.00	0.879	2.67E-01	0	0	0	0	KCNIP3
52	2:96000943	rs2024277	a	t	0.2259	0.0199	DEPR	DEPR_surv	1314	-0.122	0.112	0.89 [0.71, 1.10]	0.00	0.810	2.76E-01	0	0	0	0	KCNIP3
53	2:96000943	rs2024277	a	t	0.2400	0.0191	MMSE	MMSE_cont	2114	-0.049	0.055	-0.05 [-0.16, 0.06]	0.00	0.899	3.76E-01	0	0	0	0	KCNIP3
54	2:96000943	rs2024277	a	t	0.2208	0.0182	HYPOSIMIA	HYPOSIMIA_base	1588	0.082	0.096	1.09 [0.90, 1.31]	0.00	0.994	3.94E-01	0	0	0	0	KCNIP3
55	2:96000943	rs2024277	a	t	0.2413	0.0139	SEADL	SEADL_cont	2218	0.228	0.299	0.23 [-0.36, 0.81]	18.40	0.285	4.45E-01	0	0	0	0	KCNIP3
56	2:96000943	rs2024277	a	t	0.2250	0.0194	CONST	CONST_base	1472	-0.078	0.103	0.93 [0.76, 1.13]	40.20	0.154	4.49E-01	0	0	0	0	KCNIP3
57	2:96000943	rs2024277	a	t	0.2317	0.0208	MOTORFLUX	MOTORFLUX_surv	1709	0.048	0.065	1.05 [0.92, 1.19]	0.00	0.506	4.60E-01	0	0	0	0	KCNIP3
58	2:96000943	rs2024277	a	t	0.2364	0.0163	UPDRS1_scaled	UPDRS1_scaled_cont	2111	-0.025	0.040	-0.02 [-0.10, 0.05]	0.00	0.853	5.41E-01	0	0	0	0	KCNIP3
59	2:96000943	rs2024277	a	t	0.2325	0.0157	DYSKINESIAS	DYSKINESIAS_base	1232	-0.052	0.124	0.95 [0.74, 1.21]	51.70	0.126	6.73E-01	0	0	0	0	KCNIP3
60	2:96000943	rs2024277	a	t	0.2353	0.0143	UPDRS3_scaled	UPDRS3_scaled_cont	2446	0.011	0.034	0.01 [-0.06, 0.08]	0.00	0.448	7.56E-01	0	0	0	0	KCNIP3

1	5:60137959	rs1867598	a	g	0.8909	0.0123	MOTORFLUX	MOTORFLUX_surv	1709	0.008	0.077	1.01 [0.87, 1.17]	31.50	0.188	9.20E-01	0	0	0	0	ELOVL7
2	1:226916078	rs4653767	t	c	0.7302	0.0150	INS	INS_surv	1112	0.168	0.076	1.18 [1.02, 1.37]	0.00	0.551	2.71E-02	0	0	0	0	ITPKB
2	1:226916078	rs4653767	t	c	0.7288	0.0140	HY3	HY3_surv	2582	-0.100	0.071	0.90 [0.79, 1.04]	20.70	0.259	1.56E-01	0	0	0	0	ITPKB
3	1:226916078	rs4653767	t	c	0.7331	0.0150	COGI	COGI_base	2859	-0.131	0.098	0.88 [0.72, 1.06]	0.00	0.748	1.79E-01	0	0	0	0	ITPKB
3	1:226916078	rs4653767	t	c	0.7232	0.0173	MOTORFLUX	MOTORFLUX_base	1803	-0.102	0.091	0.90 [0.76, 1.08]	0.00	0.908	2.58E-01	0	0	0	0	ITPKB
4	1:226916078	rs4653767	t	c	0.7293	0.0179	SEADL	SEADL_cont	2218	-0.258	0.261	-0.26 [-0.77, 0.25]	22.30	0.252	3.23E-01	0	0	0	0	ITPKB
4	1:226916078	rs4653767	t	c	0.7261	0.0190	UPDRS3_scaled	UPDRS3_scaled_cont	2446	-0.024	0.029	-0.02 [-0.08, 0.03]	42.50	0.095	4.01E-01	0	0	0	0	ITPKB
5	1:226916078	rs4653767	t	c	0.7244	0.0190	DYSKINESIAS	DYSKINESIAS_base	1232	-0.088	0.114	0.92 [0.73, 1.15]	6.90	0.341	4.44E-01	0	0	0	0	ITPKB
5	1:226916078	rs4653767	t	c	0.7260	0.0170	MMSE	MMSE_cont	2114	-0.035	0.050	-0.03 [-0.13, 0.06]	0.00	0.676	4.87E-01	0	0	0	0	ITPKB
6	1:226916078	rs4653767	t	c	0.7233	0.0100	SEADL70	SEADL70_surv	1683	0.066	0.105	1.07 [0.87, 1.31]	33.70	0.196	5.27E-01	0	0	0	0	ITPKB
6	1:226916078	rs4653767	t	c	0.7390	0.0113	CONST	CONST_base	1472	0.048	0.098	1.05 [0.87, 1.27]	0.00	0.444	6.23E-01	0	0	0	0	ITPKB
7	1:226916078	rs4653767	t	c	0.7330	0.0189	COGI	COGI_surv	2244	0.036	0.085	1.04 [0.88, 1.22]	0.00	0.687	6.70E-01	0	0	0	0	ITPKB
7	1:226916078	rs4653767	t	c	0.7289	0.0191	UPDRS_scaled	UPDRS_scaled_cont	2994	-0.011	0.026	-0.01 [-0.06, 0.04]	44.10	0.065	6.89E-01	0	0	0	0	ITPKB
8	1:226916078	rs4653767	t	c	0.7236	0.0191	UPDRS1_scaled	UPDRS1_scaled_cont	2111	-0.013	0.032	-0.01 [-0.08, 0.05]	33.70	0.171	6.91E-01	0	0	0	0	ITPKB
8	1:226916078	rs4653767	t	c	0.7415	0.0186	MOCA	MOCA_cont	1074	0.053	0.137	0.05 [-0.22, 0.32]	0.00	0.743	7.02E-01	0	0	0	0	ITPKB
9	1:226916078	rs4653767	t	c	0.7266	0.0066	MOTORFLUX	MOTORFLUX_surv	1709	0.020	0.054	1.02 [0.92, 1.13]	0.00	0.890	7.07E-01	0	0	0	0	ITPKB
9	1:226916078	rs4653767	t	c	0.7323	0.0204	DEPR	DEPR_base	2138	-0.035	0.102	0.97 [0.79, 1.18]	0.00	0.603	7.31E-01	0	0	0	0	ITPKB
10	1:226916078	rs4653767	t	c	0.7334	0.0174	HY3	HY3_base	1289	-0.041	0.132	0.96 [0.74, 1.24]	0.00	0.647	7.59E-01	0	0	0	0	ITPKB
10	1:226916078	rs4653767	t	c	0.7415	0.0155	SLEEP	SLEEP_base	1724	-0.026	0.095	0.97 [0.81, 1.17]	0.00	0.644	7.86E-01	0	0	0	0	ITPKB
11	1:226916078	rs4653767	t	c	0.7232	0.0197	UPDRS2_scaled	UPDRS2_scaled_cont	2103	-0.008	0.032	-0.01 [-0.07, 0.05]	0.00	0.458	8.03E-01	0	0	0	0	ITPKB
11	1:226916078	rs4653767	t	c	0.7313	0.0206	INS	INS_base	2220	0.019	0.080	1.02 [0.87, 1.19]	6.60	0.380	8.17E-01	0	0	0	0	ITPKB
12	1:226916078	rs4653767	t	c	0.7233	0.0196	UPDRS4_scaled	UPDRS4_scaled_cont	1798	-0.006	0.028	-0.01 [-0.06, 0.05]	0.00	0.854	8.19E-01	0	0	0	0	ITPKB
12	1:226916078	rs4653767	t	c	0.7398	0.0132	HYPOSMIA	HYPOSMIA_base	1588	0.014	0.091	1.01 [0.85, 1.21]	0.00	0.552	8.77E-01	0	0	0	0	ITPKB
13	1:226916078	rs4653767	t	c	0.7330	0.0191	HY	HY_cont	3627	-0.001	0.010	-0.00 [-0.02, 0.02]	8.20	0.365	9.19E-01	0	0	0	0	ITPKB
14	17:40741013	rs12951632	t	c	0.7403	0.0083	HY3	HY3_base	1289	-0.287	0.131	0.75 [0.58, 0.97]	0.00	0.431	2.78E-02	0	0	0	0	RETREG3
14	17:40741013	rs12951632	t	c	0.7471	0.0196	HY	HY_cont	3627	-0.021	0.010	-0.02 [-0.04, -0.00]	41.90	0.062	3.47E-02	0	0	0	0	RETREG3
15	17:40741013	rs12951632	t	c	0.7499	0.0191	UPDRS3_scaled	UPDRS3_scaled_cont	2446	-0.042	0.029	-0.04 [-0.10, 0.02]	0.00	0.518	1.49E-01	0	0	0	0	RETREG3
15	17:40741013	rs12951632	t	c	0.7561	0.0117	MMSE	MMSE_cont	2114	0.059	0.052	0.06 [-0.04, 0.16]	10.00	0.353	2.55E-01	0	0	0	0	RETREG3
15	17:40741013	rs12951632	t	c	0.7523	0.0122	MOCA	MOCA_cont	1074	-0.153	0.140	-0.15 [-0.43, 0.12]	43.60	0.150	2.75E-01	0	0	0	0	RETREG3
16	17:40741013	rs12951632	t	c	0.7493	0.0212	HY3	HY3_surv	2582	-0.068	0.071	0.93 [0.81, 1.07]	0.00	0.486	3.42E-01	0	0	0	0	RETREG3
16	17:40741013	rs12951632	t	c	0.7508	0.0176	UPDRS_scaled	UPDRS_scaled_cont	2994	-0.026	0.027	-0.03 [-0.08, 0.03]	0.00	0.962	3.42E-01	0	0	0	0	RETREG3
17	17:40741013	rs12951632	t	c	0.7565	0.0158	UPDRS2_scaled	UPDRS2_scaled_cont	2103	-0.031	0.033	-0.03 [-0.10, 0.03]	0.00	0.483	3.53E-01	0	0	0	0	RETREG3
17	17:40741013	rs12951632	t	c	0.7411	0.0148	CONST	CONST_base	1472	0.091	0.099	1.10 [0.90, 1.33]	0.00	0.624	3.54E-01	0	0	0	0	RETREG3
18	17:40741013	rs12951632	t	c	0.7457	0.0182	SLEEP	SLEEP_base	1724	0.086	0.096	1.09 [0.90, 1.32]	0.00	0.495	3.70E-01	0	0	0	0	RETREG3
18	17:40741013	rs12951632	t	c	0.7436	0.0092	DYSKINESIAS	DYSKINESIAS_base	1232	-0.086	0.117	0.92 [0.73, 1.15]	0.00	0.442	4.63E-01	0	0	0	0	RETREG3
19	17:40741013	rs12951632	t	c	0.7578	0.0175	UPDRS4_scaled	UPDRS4_scaled_cont	1798	-0.018	0.029	-0.02 [-0.07, 0.04]	0.00	0.800	5.37E-01	0	0	0	0	RETREG3
19	17:40741013	rs12951632	t	c	0.7578	0.0139	SEADL	SEADL_cont	2218	-0.160	0.272	-0.16 [-0.69, 0.37]	0.00	0.707	5.57E-01	0	0	0	0	RETREG3
20	17:40741013	rs12951632	t	c	0.7585	0.0163	UPDRS1_scaled	UPDRS1_scaled_cont	2111	-0.018	0.033	-0.02 [-0.08, 0.05]	0.00	0.914	5.91E-01	0	0	0	0	RETREG3
20	17:40741013	rs12951632	t	c	0.7583	0.0189	DEPR	DEPR_base	2138	-0.047	0.104	0.95 [0.78, 1.17]	0.00	0.891	6.50E-01	0	0	0	0	RETREG3
21	17:40741013	rs12951632	t	c	0.7485	0.0178	COGI	COGI_surv	2244	0.033	0.085	1.03 [0.88, 1.22]	0.00	0.763	6.96E-01	0	0	0	0	RETREG3
21	17:40741013	rs12951632	t	c	0.7411	0.0129	COGI	COGI_base	2859	-0.031	0.098	0.97 [0.80, 1.17]	0.00	0.637	7.49E-01	0	0	0	0	RETREG3
22	17:40741013	rs12951632	t	c	0.7539	0.0200	MOTORFLUX	MOTORFLUX_surv	1709	0.013	0.055	1.01 [0.91, 1.13]	0.00	0.489	8.10E-01	0	0	0	0	RETREG3
22	17:40741013	rs12951632	t	c	0.7571	0.0188	DEPR	DEPR_surv	1314	-0.020	0.088	0.98 [0.82, 1.17]	0.00	0.949	8.22E-01	0	0	0	0	RETREG3
23	17:40741013	rs12951632	t	c	0.7544	0.0160	SEADL70	SEADL70_surv	1683	-0.020	0.104	0.98 [0.80, 1.20]	30.80	0.216	8.48E-01	0	0	0	0	RETREG3
23	17:40741013	rs12951632	t	c	0.7508	0.0169	MOTORFLUX	MOTORFLUX_base	1803	-0.009	0.094	0.99 [0.82, 1.19]	29.50	0.225	9.20E-01	0	0	0	0	RETREG3
24	17:40741013	rs12951632	t	c	0.7566	0.0182	DYSKINESIAS	DYSKINESIAS_surv	1856	-0.002	0.066	1.00 [0.88, 1.14]	0.00	0.480	9.75E-01	0	0	0	0	RETREG3
24	17:40741013	rs12951632	t	c	0.7477	0.0160	INS	INS_base	2220	0.002	0.081	1.00 [0.86, 1.17]	19.70	0.274	9.79E-01	0	0	0	0	RETREG3
25	17:40741013	rs12951632	t	c	0.7527	0.0171	INS	INS_surv	1112	-0.002	0.075	1.00 [0.86, 1.16]	26.20	0.238	9.81E-01	0	0	0	0	RETREG3
25	17:40741013	rs12951632	t	c	0.7436	0.0167	HYPOSMIA	HYPOSMIA_base	1588	-0.002	0.091	1.00 [0.84, 1.19]	40.00	0.139	9.86E-01	0	0	0	0	RETREG3
26	5:134199105	rs11950533	a	c	0.0987	0.0110	MOTORFLUX	MOTORFLUX_surv	1709	-0.185	0.085	0.83 [0.70, 0.98]	0.00	0.681	2.98E-02	0	0	0	0	C5orf24
26	5:134199105	rs11950533	a	c	0.0955	0.0114	DYSKINESIAS	DYSKINESIAS_surv	1856	-0.228	0.105	0.80 [0.65, 0.98]	38.40	0.136	3.00E-02	0	0	0	0	C5orf24
27	5:134199105	rs11950533	a	c	0.0904	0.0110	UPDRS4_scaled	UPDRS4_scaled_cont	1798	-0.085	0.045	-0.09 [-0.17, 0.00]	0.00	0.940	5.65E-02	0	0	0	0	C5orf24
27	5:134199105	rs11950533	a	c	0.1050	0.0025	HY3	HY3_base	1289	-0.371	0.211	0.69 [0.46, 1.04]	0.00	0.796	7.87E-02	0	0	0	0	C5orf24
28	5:134199105	rs11950533	a	c	0.0939	0.0133	UPDRS3_scaled	UPDRS3_scaled_cont	2446	0.069	0.044	0.07 [-0.02, 0.16]	1.10	0.421	1.20E-01	0	0	0	0	C5orf24
28	5:134199105	rs11950533	a	c	0.0990	0.0136	CONST	CONST_base	1472	-0.227	0.149	0.80 [0.59, 1.07]	0.00	0.712	1.28E-01	0	0	0	0	C5orf24
29	5:134199105	rs11950533	a	c	0.1008	0.0071	HY3	HY3_surv	2582	0.136	0.101	1.15 [0.94, 1.40]	14.80	0.310	1.77E-01	0	0	0	0	C5orf24
29	5:134199105	rs11950533	a	c	0.0988	0.0147	SEADL	SEADL_cont	2218	0.500	0.395	0.50 [-0.27, 1.27]	0.00	0.713	2.06E-01	0	0	0	0	C5orf24
30	5:134199105	rs11950533	a	c	0.0951	0.0123	UPDRS_scaled	UPDRS_scaled_cont	2994	-0.051	0.041	-0.05 [-0.13, 0.03]	26.50	0.200	2.12E-01	0	0	0	0	C5orf24
30	5:134199105	rs11950533	a	c	0.1003	0.0126	DEPR	DEPR_surv	1314	0.143	0.132	1.15 [0.89, 1.49]	0.00	0.724	2.78E-01	0	0	0	0	C5orf24
31	5:134199105	rs11950533	a	c	0.1004	0.0127	MOCA	MOCA_cont	1074	0.200	0.198	0.20 [-0.19, 0.59]	0.00	0.577	3.14E-01	0	0	0	0	C5orf24
31	5:134199105	rs11950533	a	c	0.0976	0.0104	COGI	COGI_surv	2244	0.122	0.125									

1	3:161077630	rs1450522	a	g	0.6677	0.0328	UPDRS2_scaled	UPDRS2_scaled_cont	2103	-0.015	0.031	-0.02 [-0.08, 0.04]	11.10	0.345	6.17E-01	0	0	0	0	SPTSSB
2	3:161077630	rs1450522	a	g	0.6750	0.0121	HY3	HY3_base	1289	0.035	0.124	1.04 [0.81, 1.32]	0.00	0.532	7.76E-01	0	0	0	0	SPTSSB
3	3:161077630	rs1450522	a	g	0.6725	0.0195	COGI	COGI_surv	2244	0.021	0.078	1.02 [0.88, 1.19]	0.00	0.975	7.85E-01	0	0	0	0	SPTSSB
4	3:161077630	rs1450522	a	g	0.6843	0.0152	HYPOSIMIA	HYPOSIMIA_base	1588	-0.023	0.087	0.98 [0.82, 1.16]	0.00	0.753	7.88E-01	0	0	0	0	SPTSSB
5	3:161077630	rs1450522	a	g	0.6669	0.0232	INS	INS_surv	1112	0.019	0.070	1.02 [0.89, 1.17]	0.00	0.489	7.93E-01	0	0	0	0	SPTSSB
6	3:161077630	rs1450522	a	g	0.6711	0.0140	MOTORFLUX	MOTORFLUX_base	1803	0.019	0.087	1.02 [0.86, 1.21]	45.00	0.122	8.28E-01	0	0	0	0	SPTSSB
7	3:161077630	rs1450522	a	g	0.6707	0.0107	SEADL70	SEADL70_surv	1683	-0.018	0.095	0.98 [0.82, 1.18]	0.00	0.461	8.49E-01	0	0	0	0	SPTSSB
8	3:161077630	rs1450522	a	g	0.6859	0.0152	SLEEP	SLEEP_base	1724	-0.011	0.091	0.99 [0.83, 1.18]	36.80	0.148	9.05E-01	0	0	0	0	SPTSSB
9	3:161077630	rs1450522	a	g	0.6732	0.0282	UPDRS_scaled	UPDRS_scaled_cont	2994	-0.002	0.025	-0.00 [-0.05, 0.05]	0.00	0.572	9.36E-01	0	0	0	0	SPTSSB
10	3:161077630	rs1450522	a	g	0.6741	0.0110	COGI	COGI_base	2859	-0.006	0.092	0.99 [0.83, 1.19]	0.00	0.730	9.49E-01	0	0	0	0	SPTSSB
11	3:151108965	rs11707416	a	t	0.3743	0.0109	DYSKINESIAS	DYSKINESIAS_base	1232	0.228	0.107	1.26 [1.02, 1.55]	0.00	0.611	3.35E-02	0	0	0	0	MED12L
12	3:151108965	rs11707416	a	t	0.3462	0.0268	SEADL	SEADL_cont	2218	0.403	0.250	0.40 [-0.09, 0.89]	0.00	0.687	1.06E-01	0	0	0	0	MED12L
13	3:151108965	rs11707416	a	t	0.3548	0.0265	SEADL70	SEADL70_surv	1683	-0.118	0.097	0.89 [0.74, 1.07]	0.00	0.485	2.22E-01	0	0	0	0	MED12L
14	3:151108965	rs11707416	a	t	0.3681	0.0161	MOTORFLUX	MOTORFLUX_base	1803	0.085	0.084	1.09 [0.92, 1.28]	0.00	0.417	3.14E-01	0	0	0	0	MED12L
15	3:151108965	rs11707416	a	t	0.3605	0.0263	INS	INS_surv	1112	0.068	0.070	1.07 [0.93, 1.23]	0.00	0.887	3.35E-01	0	0	0	0	MED12L
16	3:151108965	rs11707416	a	t	0.3721	0.0133	HYPOSIMIA	HYPOSIMIA_base	1588	-0.075	0.083	0.93 [0.79, 1.09]	38.60	0.149	3.68E-01	0	0	0	0	MED12L
17	3:151108965	rs11707416	a	t	0.3678	0.0203	UPDRS4_scaled	UPDRS4_scaled_cont	1798	0.022	0.026	0.02 [-0.03, 0.07]	0.00	0.874	3.90E-01	0	0	0	0	MED12L
18	3:151108965	rs11707416	a	t	0.3584	0.0273	UPDRS3_scaled	UPDRS3_scaled_cont	2446	-0.020	0.027	-0.02 [-0.07, 0.03]	0.00	0.516	4.54E-01	0	0	0	0	MED12L
19	3:151108965	rs11707416	a	t	0.3713	0.0116	INS	INS_base	2220	0.051	0.073	1.05 [0.91, 1.21]	0.00	0.758	4.84E-01	0	0	0	0	MED12L
20	3:151108965	rs11707416	a	t	0.3533	0.0326	DEPR	DEPR_surv	1314	-0.051	0.085	0.95 [0.81, 1.12]	29.20	0.216	5.49E-01	0	0	0	0	MED12L
21	3:151108965	rs11707416	a	t	0.3750	0.0119	CONST	CONST_base	1472	-0.049	0.088	0.95 [0.80, 1.13]	0.00	0.442	5.76E-01	0	0	0	0	MED12L
22	3:151108965	rs11707416	a	t	0.3740	0.0129	SLEEP	SLEEP_base	1724	0.046	0.085	1.05 [0.89, 1.24]	2.60	0.405	5.92E-01	0	0	0	0	MED12L
23	3:151108965	rs11707416	a	t	0.3610	0.0263	COGI	COGI_surv	2244	0.039	0.079	1.04 [0.89, 1.21]	0.00	0.664	6.19E-01	0	0	0	0	MED12L
24	3:151108965	rs11707416	a	t	0.3493	0.0310	MOTORFLUX	MOTORFLUX_surv	1709	-0.025	0.052	0.97 [0.88, 1.08]	0.00	0.826	6.27E-01	0	0	0	0	MED12L
25	3:151108965	rs11707416	a	t	0.3647	0.0194	COGI	COGI_base	2859	-0.038	0.091	0.96 [0.81, 1.15]	42.70	0.094	6.75E-01	0	0	0	0	MED12L
26	3:151108965	rs11707416	a	t	0.3620	0.0276	UPDRS2_scaled	UPDRS2_scaled_cont	2103	-0.012	0.031	-0.01 [-0.07, 0.05]	37.40	0.144	7.02E-01	0	0	0	0	MED12L
27	3:151108965	rs11707416	a	t	0.3732	0.0123	HY3	HY3_base	1289	-0.047	0.123	0.95 [0.75, 1.21]	0.00	0.932	7.02E-01	0	0	0	0	MED12L
28	3:151108965	rs11707416	a	t	0.3589	0.0294	UPDRS1_scaled	UPDRS1_scaled_cont	2111	0.011	0.030	0.01 [-0.05, 0.07]	0.00	0.501	7.09E-01	0	0	0	0	MED12L
29	3:151108965	rs11707416	a	t	0.3574	0.0328	MOCA	MOCA_cont	1074	-0.048	0.130	-0.05 [-0.30, 0.21]	42.00	0.160	7.10E-01	0	0	0	0	MED12L
30	3:151108965	rs11707416	a	t	0.3562	0.0226	HY3	HY3_surv	2582	-0.008	0.064	0.99 [0.87, 1.13]	0.00	0.651	9.04E-01	0	0	0	0	MED12L
31	3:151108965	rs11707416	a	t	0.3517	0.0248	DYSKINESIAS	DYSKINESIAS_surv	1856	0.002	0.061	1.00 [0.89, 1.13]	18.20	0.291	9.78E-01	0	0	0	0	MED12L
32	17:43744203	rs62053943	t	c	0.1336	0.0211	HYPOSIMIA	HYPOSIMIA_base	1588	0.249	0.118	1.28 [1.02, 1.62]	0.00	0.992	3.47E-02	0	0	0	0	CRHRI
33	17:43744203	rs62053943	t	c	0.1269	0.0129	MOTORFLUX	MOTORFLUX_base	1803	-0.247	0.126	0.78 [0.61, 1.00]	0.00	0.697	5.03E-02	0	0	0	0	CRHRI
34	17:43744203	rs62053943	t	c	0.1259	0.0192	SEADL70	SEADL70_surv	1683	0.268	0.138	1.31 [1.00, 1.71]	19.10	0.293	5.24E-02	0	0	0	0	CRHRI
35	17:43744203	rs62053943	t	c	0.1377	0.0132	HY3	HY3_base	1289	-0.343	0.183	0.71 [0.50, 1.02]	0.00	0.510	6.07E-02	0	0	0	0	CRHRI
36	17:43744203	rs62053943	t	c	0.1327	0.0207	SLEEP	SLEEP_base	1724	0.192	0.120	1.21 [0.96, 1.53]	3.10	0.402	1.08E-01	0	0	0	0	CRHRI
37	17:43744203	rs62053943	t	c	0.1347	0.0194	MOTORFLUX	MOTORFLUX_surv	1709	-0.105	0.071	0.90 [0.78, 1.04]	0.00	0.437	1.41E-01	0	0	0	0	CRHRI
38	17:43744203	rs62053943	t	c	0.1387	0.0135	CONST	CONST_base	1472	-0.148	0.123	0.86 [0.68, 1.10]	24.20	0.260	2.28E-01	0	0	0	0	CRHRI
39	17:43744203	rs62053943	t	c	0.1279	0.0194	COGI	COGI_base	2859	-0.151	0.136	0.86 [0.66, 1.12]	0.60	0.424	2.66E-01	0	0	0	0	CRHRI
40	17:43744203	rs62053943	t	c	0.1318	0.0191	DEPR	DEPR_surv	1314	-0.128	0.119	0.88 [0.70, 1.11]	44.80	0.107	2.85E-01	0	0	0	0	CRHRI
41	17:43744203	rs62053943	t	c	0.1348	0.0199	HY3	HY3_surv	2582	0.094	0.091	1.10 [0.92, 1.31]	0.00	0.557	3.05E-01	0	0	0	0	CRHRI
42	17:43744203	rs62053943	t	c	0.1134	0.0138	UPDRS1_scaled	UPDRS1_scaled_cont	2111	0.040	0.045	0.04 [-0.05, 0.13]	0.00	0.435	3.81E-01	0	0	0	0	CRHRI
43	17:43744203	rs62053943	t	c	0.1298	0.0198	HY3	HY3_cont	3627	-0.011	0.013	-0.01 [-0.04, 0.01]	49.00	0.397	4.17E-01	0	0	0	0	CRHRI
44	17:43744203	rs62053943	t	c	0.1301	0.0112	DYSKINESIAS	DYSKINESIAS_base	1232	0.113	0.151	1.12 [0.83, 1.50]	0.00	0.398	4.55E-01	0	0	0	0	CRHRI
45	17:43744203	rs62053943	t	c	0.1300	0.0216	DYSKINESIAS	DYSKINESIAS_surv	1856	-0.054	0.086	0.95 [0.80, 1.12]	5.20	0.387	5.30E-01	0	0	0	0	CRHRI
46	17:43744203	rs62053943	t	c	0.1314	0.0194	INS	INS_base	2220	0.063	0.104	1.06 [0.87, 1.30]	0.00	0.436	5.45E-01	0	0	0	0	CRHRI
47	17:43744203	rs62053943	t	c	0.1315	0.0268	COGI	COGI_surv	2244	-0.066	0.115	0.94 [0.75, 1.17]	31.60	0.165	5.69E-01	0	0	0	0	CRHRI
48	17:43744203	rs62053943	t	c	0.1185	0.0169	UPDRS_scaled	UPDRS_scaled_cont	2994	-0.017	0.036	-0.02 [-0.09, 0.05]	38.70	0.100	6.28E-01	0	0	0	0	CRHRI
49	17:43744203	rs62053943	t	c	0.1111	0.0140	UPDRS4_scaled	UPDRS4_scaled_cont	1798	-0.015	0.040	-0.02 [-0.09, 0.06]	0.00	0.534	7.05E-01	0	0	0	0	CRHRI
50	17:43744203	rs62053943	t	c	0.1356	0.0211	INS	INS_surv	1112	-0.027	0.097	0.97 [0.80, 1.18]	0.00	0.741	7.82E-01	0	0	0	0	CRHRI
51	17:43744203	rs62053943	t	c	0.1274	0.0131	DEPR	DEPR_base	2138	-0.033	0.138	0.97 [0.74, 1.27]	34.00	0.157	8.12E-01	0	0	0	0	CRHRI
52	17:43744203	rs62053943	t	c	0.1250	0.0214	SEADL	SEADL_cont	2218	0.070	0.351	0.07 [-0.62, 0.76]	0.00	0.774	8.41E-01	0	0	0	0	CRHRI
53	17:43744203	rs62053943	t	c	0.1301	0.0245	MOCA	MOCA_cont	1074	-0.003	0.175	-0.00 [-0.35, 0.34]	0.00	0.921	9.86E-01	0	0	0	0	CRHRI
54	12:05723572	rs823118	t	c	0.5740	0.0192	UPDRS2_scaled	UPDRS2_scaled_cont	2103	-0.061	0.029	-0.06 [-0.12, -0.00]	0.00	0.851	3.60E-02	0	0	0	0	NUCKS1
55	12:05723572	rs823118	t	c	0.5688	0.0211	UPDRS4_scaled	UPDRS4_scaled_cont	1798	0.051	0.025	0.05 [0.00, 0.10]	11.00	0.345	4.27E-02	0	0	0	0	NUCKS1
56	12:05723572	rs823118	t	c	0.5769	0.0260	HY3	HY3_surv	2582	-0.120	0.062	0.89 [0.79, 1.00]	0.00	0.452	5.30E-02	0	0	0	0	NUCKS1
57	12:05723572	rs823118	t	c	0.5811	0.0135	HYPOSIMIA	HYPOSIMIA_base	1588	-0.095	0.082	0.91 [0.77, 1.07]	0.00	0.688	2.46E-01	0	0	0	0	NUCKS1
58	12:05723572	rs823118	t	c	0.5801	0.0199	COGI	COGI_surv	2244	-0.075	0.075	0.93 [0.80, 1.07]	0.00	0.860	3.16E-01	0	0	0	0	NUCKS1
59	12:05723572	rs823118	t	c	0.5760	0.0195	UPDRS3_scaled	UPDRS3_scaled_cont	2446	-0.026	0.026	-0.03 [-0.08, 0.02]	0.00	0.728	3.18E-01	0	0	0	0	NUCKS1
60	12:05723572	rs823118	t	c	0.5858	0.0196	CONST	CONST_base	1472	0.076	0.088	1.08 [0.91, 1.28]	0.00	0.735	3.87E-01	0	0	0	0	NUCKS1
61	12:0																			

1	3:18361759	rs73038319	a	c	0.9581	0.0092	MOTORFLUX	MOTORFLUX_base	1803	0.051	0.212	1.05 [0.69, 1.60]	41.00	0.148	8.10E-01	0	0	0	0	SATB1
2	3:18361759	rs73038319	a	c	0.9572	0.0097	UPDRS4_scaled	UPDRS4_scaled_cont	1798	0.012	0.062	0.01 [-0.11, 0.13]	0.00	0.939	8.42E-01	0	0	0	0	SATB1
3	3:18361759	rs73038319	a	c	0.9515	0.0006	COGI	COGI_surv	2148	0.032	0.169	1.03 [0.74, 1.44]	0.00	0.939	8.49E-01	0	0	0	0	SATB1
3	3:18361759	rs73038319	a	c	0.9504	0.0120	UPDRS3_scaled	UPDRS3_scaled_cont	2446	-0.011	0.061	-0.01 [-0.13, 0.11]	27.60	0.209	8.63E-01	0	0	0	0	SATB1
3	3:18361759	rs73038319	a	c	0.9493	0.0087	HY3	HY3_surv	2582	0.024	0.147	1.02 [0.77, 1.37]	0.00	0.490	8.69E-01	0	0	0	0	SATB1
4	3:18361759	rs73038319	a	c	0.9527	0.0099	HY3	HY3_base	1289	-0.038	0.258	0.96 [0.58, 1.60]	0.00	0.824	8.83E-01	0	0	0	0	SATB1
4	3:18361759	rs73038319	a	c	0.9502	0.0047	MOCA	MOCA_cont	1026	-0.039	0.285	-0.04 [-0.60, 0.52]	0.00	0.667	8.92E-01	0	0	0	0	SATB1
5	3:18361759	rs73038319	a	c	0.9526	0.0084	COGI	COGI_base	2859	-0.027	0.197	0.97 [0.66, 1.43]	0.00	0.634	8.92E-01	0	0	0	0	SATB1
5	3:18361759	rs73038319	a	c	0.9444	0.0083	DEPR	DEPR_surv	1177	-0.010	0.186	0.99 [0.69, 1.43]	0.00	0.937	9.58E-01	0	0	0	0	SATB1
6	6:27738801	rs4140646	a	g	0.2512	0.0209	DEPR	DEPR_surv	1314	-0.186	0.090	0.83 [0.70, 0.99]	0.00	0.845	9.39E-02	0	0	0	0	LOC100131289
6	6:27738801	rs4140646	a	g	0.2371	0.0268	COGI	COGI_surv	2244	-0.159	0.088	0.85 [0.72, 1.01]	0.00	0.503	7.03E-02	0	0	0	0	LOC100131289
7	6:27738801	rs4140646	a	g	0.2465	0.0244	HY3	HY3_surv	2582	-0.104	0.073	0.90 [0.78, 1.04]	14.10	0.317	1.51E-01	0	0	0	0	LOC100131289
7	6:27738801	rs4140646	a	g	0.2309	0.0131	SEADL	SEADL_cont	2218	-0.342	0.272	-0.34 [-0.88, 0.19]	0.00	0.824	2.09E-01	0	0	0	0	LOC100131289
8	6:27738801	rs4140646	a	g	0.2310	0.0168	UPDRS3_scaled	UPDRS3_scaled_cont	2446	0.037	0.030	0.04 [-0.02, 0.10]	47.60	0.064	2.16E-01	0	0	0	0	LOC100131289
8	6:27738801	rs4140646	a	g	0.2396	0.0200	SLEEP	SLEEP_base	1724	0.113	0.096	1.12 [0.93, 1.35]	0.00	0.549	2.40E-01	0	0	0	0	LOC100131289
9	6:27738801	rs4140646	a	g	0.2341	0.0294	HY3	HY3_base	1289	0.152	0.140	1.16 [0.89, 1.53]	43.40	0.171	2.76E-01	0	0	0	0	LOC100131289
9	6:27738801	rs4140646	a	g	0.2284	0.0187	UPDRS1_scaled	UPDRS1_scaled_cont	2111	-0.035	0.034	-0.03 [-0.10, 0.03]	9.00	0.360	3.14E-01	0	0	0	0	LOC100131289
10	6:27738801	rs4140646	a	g	0.2364	0.0248	UPDRS_scaled	UPDRS_scaled_cont	2994	0.026	0.028	0.03 [-0.03, 0.08]	7.70	0.371	3.40E-01	0	0	0	0	LOC100131289
10	6:27738801	rs4140646	a	g	0.2401	0.0227	MOTORFLUX	MOTORFLUX_surv	1709	-0.053	0.057	0.95 [0.85, 1.06]	0.00	0.633	3.46E-01	0	0	0	0	LOC100131289
11	6:27738801	rs4140646	a	g	0.2270	0.0112	SEADL70	SEADL70_surv	1683	0.091	0.102	1.10 [0.90, 1.34]	0.00	0.913	3.72E-01	0	0	0	0	LOC100131289
11	6:27738801	rs4140646	a	g	0.2407	0.0208	DEPR	DEPR_base	2138	-0.089	0.108	0.91 [0.74, 1.13]	19.60	0.274	4.09E-01	0	0	0	0	LOC100131289
12	6:27738801	rs4140646	a	g	0.2300	0.0207	INS	INS_base	2220	0.068	0.083	1.07 [0.91, 1.26]	0.00	0.578	4.15E-01	0	0	0	0	LOC100131289
12	6:27738801	rs4140646	a	g	0.2270	0.0203	UPDRS2_scaled	UPDRS2_scaled_cont	2103	0.022	0.035	0.02 [-0.05, 0.09]	0.00	0.776	5.17E-01	0	0	0	0	LOC100131289
13	6:27738801	rs4140646	a	g	0.2248	0.0245	MOTORFLUX	MOTORFLUX_base	1803	-0.058	0.098	0.94 [0.78, 1.14]	44.40	0.126	5.53E-01	0	0	0	0	LOC100131289
13	6:27738801	rs4140646	a	g	0.2340	0.0285	INS	INS_surv	1112	-0.038	0.075	0.96 [0.83, 1.11]	0.00	0.824	6.10E-01	0	0	0	0	LOC100131289
14	6:27738801	rs4140646	a	g	0.2256	0.0189	UPDRS4_scaled	UPDRS4_scaled_cont	1798	0.015	0.030	0.01 [-0.04, 0.07]	9.00	0.358	6.17E-01	0	0	0	0	LOC100131289
14	6:27738801	rs4140646	a	g	0.2337	0.0253	COGI	COGI_base	2859	-0.050	0.104	0.95 [0.78, 1.17]	44.10	0.085	6.29E-01	0	0	0	0	LOC100131289
15	6:27738801	rs4140646	a	g	0.2329	0.0163	MOCA	MOCA_cont	1074	-0.063	0.140	-0.06 [-0.34, 0.21]	0.00	0.997	6.52E-01	0	0	0	0	LOC100131289
15	6:27738801	rs4140646	a	g	0.2378	0.0213	CONST	CONST_base	1472	0.033	0.098	1.03 [0.85, 1.25]	31.20	0.213	7.34E-01	0	0	0	0	LOC100131289
16	6:27738801	rs4140646	a	g	0.2329	0.0151	DYSKINESIAS	DYSKINESIAS_surv	1856	-0.022	0.069	0.98 [0.85, 1.12]	45.90	0.086	7.45E-01	0	0	0	0	LOC100131289
16	6:27738801	rs4140646	a	g	0.2371	0.0185	HYPOSMIA	HYPOSMIA_base	1588	-0.011	0.094	0.99 [0.82, 1.19]	0.00	0.826	9.11E-01	0	0	0	0	LOC100131289
17	6:27738801	rs4140646	a	g	0.2300	0.0279	MMSE	MMSE_cont	2114	0.003	0.053	0.00 [-0.10, 0.11]	0.00	0.767	9.49E-01	0	0	0	0	LOC100131289
17	16:52969426	rs10221156	a	g	0.0793	0.0095	HY	HY_cont	2077	-0.045	0.022	-0.05 [-0.09, -0.00]	0.00	0.951	3.93E-02	0	0	0	0	CHD9
18	16:52969426	rs10221156	a	g	0.0834	0.0149	INS	INS_base	1033	0.156	0.196	1.17 [0.80, 1.71]	38.60	0.164	4.27E-01	0	0	0	0	CHD9
18	16:52969426	rs10221156	a	g	0.0787	0.0144	SLEEP	SLEEP_base	1033	-0.175	0.221	0.84 [0.54, 1.29]	14.10	0.325	4.27E-01	0	0	0	0	CHD9
19	16:52969426	rs10221156	a	g	0.0869	0.0118	COGI	COGI_surv	1132	-0.122	0.200	0.88 [0.60, 1.31]	25.80	0.249	5.40E-01	0	0	0	0	CHD9
19	16:52969426	rs10221156	a	g	0.0825	0.0067	MMSE	MMSE_cont	1066	-0.031	0.102	-0.03 [-0.23, 0.17]	0.00	0.863	7.61E-01	0	0	0	0	CHD9
20	16:52969426	rs10221156	a	g	0.0852	0.0134	HY3	HY3_surv	1299	-0.017	0.137	0.98 [0.75, 1.29]	0.00	0.975	9.03E-01	0	0	0	0	CHD9
20	16:52969426	rs10221156	a	g	0.0784	0.0140	COGI	COGI_base	1538	-0.011	0.235	0.99 [0.62, 1.57]	23.50	0.264	9.63E-01	0	0	0	0	CHD9
21	16:52969426	rs10221156	a	g	0.0770	0.0075	UPDRS_scaled	UPDRS_scaled_cont	1108	0.000	0.073	-0.00 [-0.14, 0.14]	0.00	0.985	9.99E-01	0	0	0	0	CHD9
22	16:52636242	rs3104783	a	c	0.4252	0.0193	CONST	CONST_base	1472	-0.172	0.086	0.84 [0.71, 1.00]	0.00	0.977	4.55E-02	0	0	0	0	CASC16
22	16:52636242	rs3104783	a	c	0.4280	0.0308	HY3	HY3_base	1289	-0.148	0.119	0.86 [0.68, 1.09]	24.40	0.267	2.17E-01	0	0	0	0	CASC16
23	16:52636242	rs3104783	a	c	0.4403	0.0238	MOTORFLUX	MOTORFLUX_base	1803	0.102	0.083	1.11 [0.94, 1.30]	0.00	0.514	2.18E-01	0	0	0	0	CASC16
23	16:52636242	rs3104783	a	c	0.4253	0.0251	SLEEP	SLEEP_base	1724	0.094	0.084	1.10 [0.93, 1.29]	0.00	0.566	2.64E-01	0	0	0	0	CASC16
23	16:52636242	rs3104783	a	c	0.4360	0.0204	DEPR	DEPR_base	2138	-0.096	0.090	0.91 [0.76, 1.08]	0.00	0.792	2.88E-01	0	0	0	0	CASC16
24	16:52636242	rs3104783	a	c	0.4394	0.0265	UPDRS4_scaled	UPDRS4_scaled_cont	1798	0.021	0.025	0.02 [-0.03, 0.07]	5.50	0.382	4.09E-01	0	0	0	0	CASC16
24	16:52636242	rs3104783	a	c	0.4380	0.0130	SEADL70	SEADL70_surv	1683	0.066	0.090	1.07 [0.89, 1.27]	16.40	0.310	4.68E-01	0	0	0	0	CASC16
25	16:52636242	rs3104783	a	c	0.4226	0.0256	HYPOSMIA	HYPOSMIA_base	1588	-0.055	0.082	0.95 [0.81, 1.11]	0.00	0.451	4.98E-01	0	0	0	0	CASC16
25	16:52636242	rs3104783	a	c	0.4346	0.0285	INS	INS_base	2220	-0.044	0.071	0.96 [0.83, 1.10]	13.10	0.328	5.32E-01	0	0	0	0	CASC16
26	16:52636242	rs3104783	a	c	0.4343	0.0217	INS	INS_surv	1112	0.034	0.064	1.03 [0.91, 1.17]	0.00	0.747	5.96E-01	0	0	0	0	CASC16
26	16:52636242	rs3104783	a	c	0.4433	0.0243	UPDRS_scaled	UPDRS_scaled_cont	2994	0.012	0.024	0.01 [-0.03, 0.06]	0.00	0.463	6.17E-01	0	0	0	0	CASC16
27	16:52636242	rs3104783	a	c	0.4330	0.0246	DEPR	DEPR_surv	1314	0.025	0.078	1.03 [0.88, 1.19]	0.00	0.767	7.50E-01	0	0	0	0	CASC16
27	16:52636242	rs3104783	a	c	0.4256	0.0342	UPDRS3_scaled	UPDRS3_scaled_cont	2446	-0.008	0.026	-0.01 [-0.06, 0.04]	0.00	0.826	7.70E-01	0	0	0	0	CASC16
28	16:52636242	rs3104783	a	c	0.4216	0.0285	HY3	HY3_surv	2582	-0.018	0.061	0.98 [0.87, 1.11]	33.10	0.153	7.75E-01	0	0	0	0	CASC16
28	16:52636242	rs3104783	a	c	0.4358	0.0293	HY	HY_cont	3627	-0.002	0.009	-0.00 [-0.02, 0.02]	31.60	0.138	8.01E-01	0	0	0	0	CASC16
29	16:52636242	rs3104783	a	c	0.4394	0.0262	UPDRS2_scaled	UPDRS2_scaled_cont	2103	0.006	0.029	0.01 [-0.05, 0.06]	0.00	0.578	8.25E-01	0	0	0	0	CASC16
29	16:52636242	rs3104783	a	c	0.4325	0.0239	SEADL	SEADL_cont	2218	-0.051	0.234	-0.05 [-0.51, 0.41]	0.00	0.975	8.26E-01	0	0	0	0	CASC16
30	16:52636242	rs3104783	a	c	0.4373	0.0284	COGI	COGI_base	2859	-0.018	0.088	1.02 [0.86, 1.21]	38.10	0.126	8.40E-01	0	0	0	0	CASC16
30	16:52636242	rs3104783	a	c	0.4396	0.0249	UPDRS1_scaled	UPDRS1_scaled_cont	2111	-0.005	0.029	-0.00 [-0.06, 0.05]	0.00	0.779	8.72E-01	0	0	0	0	CASC16
31	16:52636242	rs3104783	a	c	0.4290	0.0179	MOCA	MOCA_cont	1074	-0.016	0.120	-0.02 [-0.25, 0.22]	42.70	0.155	8.95E-01	0	0	0	0	CASC16

1	1:171719769	rs11578699	t	c	0.1853	0.0182	INS	INS_base	2220	0.106	0.091	1.11 [0.93, 1.33]	0.00	0.472	2.42E-01	0	0	0	0	VAMP4
2	1:171719769	rs11578699	t	c	0.1944	0.0211	SEADL70	SEADL70_surv	1683	-0.122	0.121	0.88 [0.70, 1.12]	0.00	0.945	3.11E-01	0	0	0	0	VAMP4
3	1:171719769	rs11578699	t	c	0.1849	0.0191	HY	HY_cont	3627	0.010	0.011	0.01 [-0.01, 0.03]	0.00	0.698	3.85E-01	0	0	0	0	VAMP4
4	1:171719769	rs11578699	t	c	0.1868	0.0254	UPDRS3_scaled	UPDRS3_scaled_cont	2446	-0.024	0.033	-0.02 [-0.09, 0.04]	22.30	0.252	4.61E-01	0	0	0	0	VAMP4
5	1:171719769	rs11578699	t	c	0.1825	0.0168	SLEEP	SLEEP_base	1724	0.078	0.108	1.08 [0.88, 1.33]	0.00	0.915	4.70E-01	0	0	0	0	VAMP4
6	1:171719769	rs11578699	t	c	0.1877	0.0237	SEADL	SEADL_cont	2218	-0.207	0.297	-0.21 [-0.79, 0.38]	0.00	0.442	4.87E-01	0	0	0	0	VAMP4
7	1:171719769	rs11578699	t	c	0.1803	0.0185	MMSE	MMSE_cont	2114	-0.037	0.057	-0.04 [-0.15, 0.08]	35.30	0.146	5.23E-01	0	0	0	0	VAMP4
8	1:171719769	rs11578699	t	c	0.1902	0.0188	DEPR	DEPR_base	2138	0.064	0.113	1.07 [0.85, 1.33]	7.70	0.371	5.71E-01	0	0	0	0	VAMP4
9	1:171719769	rs11578699	t	c	0.1887	0.0115	DYSKINESIAS	DYSKINESIAS_base	1232	0.062	0.131	1.06 [0.82, 1.38]	0.00	0.845	6.36E-01	0	0	0	0	VAMP4
10	1:171719769	rs11578699	t	c	0.1818	0.0114	CONST	CONST_base	1472	-0.044	0.110	0.96 [0.77, 1.19]	0.00	0.775	6.88E-01	0	0	0	0	VAMP4
11	1:171719769	rs11578699	t	c	0.1833	0.0191	COGI	COGI_base	2859	0.040	0.113	1.04 [0.83, 1.30]	3.60	0.403	7.23E-01	0	0	0	0	VAMP4
12	1:171719769	rs11578699	t	c	0.1822	0.0128	HY3	HY3_base	1289	0.053	0.150	1.05 [0.79, 1.41]	0.00	0.952	7.24E-01	0	0	0	0	VAMP4
13	1:171719769	rs11578699	t	c	0.1928	0.0220	UPDRS2_scaled	UPDRS2_scaled_cont	2103	-0.012	0.037	-0.01 [-0.08, 0.06]	0.00	0.693	7.46E-01	0	0	0	0	VAMP4
14	1:171719769	rs11578699	t	c	0.1939	0.0219	UPDRS1_scaled	UPDRS1_scaled_cont	2111	-0.009	0.037	-0.01 [-0.08, 0.06]	18.10	0.292	8.08E-01	0	0	0	0	VAMP4
15	1:171719769	rs11578699	t	c	0.1828	0.0152	DEPR	DEPR_surv	1314	0.019	0.099	1.02 [0.84, 1.24]	0.00	0.683	8.50E-01	0	0	0	0	VAMP4
16	1:171719769	rs11578699	t	c	0.1952	0.0178	MOTORFLUX	MOTORFLUX_base	1803	0.017	0.105	1.02 [0.83, 1.25]	42.60	0.137	8.76E-01	0	0	0	0	VAMP4
17	1:171719769	rs11578699	t	c	0.1844	0.0196	COGI	COGI_surv	2244	-0.009	0.096	0.99 [0.82, 1.20]	6.70	0.380	9.23E-01	0	0	0	0	VAMP4
18	1:171719769	rs11578699	t	c	0.1848	0.0224	UPDRS_scaled	UPDRS_scaled_cont	2994	0.003	0.030	0.00 [-0.06, 0.06]	0.00	0.851	9.28E-01	0	0	0	0	VAMP4
19	6:30108683	rs9261484	t	c	0.2458	0.0127	HY3	HY3_base	1289	0.261	0.133	1.30 [1.00, 1.68]	0.00	0.536	5.01E-02	0	0	0	0	TRIM40
20	6:30108683	rs9261484	t	c	0.2403	0.0286	UPDRS1_scaled	UPDRS1_scaled_cont	2111	0.064	0.033	0.06 [-0.00, 0.13]	0.00	0.703	5.25E-02	0	0	0	0	TRIM40
21	6:30108683	rs9261484	t	c	0.2411	0.0202	COGI	COGI_surv	2244	0.147	0.083	1.16 [0.98, 1.36]	0.00	0.593	7.84E-02	0	0	0	0	TRIM40
22	6:30108683	rs9261484	t	c	0.2339	0.0083	SEADL70	SEADL70_surv	1683	0.165	0.102	1.18 [0.96, 1.44]	0.00	0.930	1.08E-01	0	0	0	0	TRIM40
23	6:30108683	rs9261484	t	c	0.2386	0.0260	SLEEP	SLEEP_base	1724	-0.151	0.097	0.86 [0.71, 1.04]	0.00	0.901	1.18E-01	0	0	0	0	TRIM40
24	6:30108683	rs9261484	t	c	0.2353	0.0104	MOCA	MOCA_cont	1074	-0.209	0.137	-0.21 [-0.48, 0.06]	0.00	0.778	1.28E-01	0	0	0	0	TRIM40
25	6:30108683	rs9261484	t	c	0.2392	0.0260	SEADL	SEADL_cont	2218	-0.375	0.269	-0.37 [-0.90, 0.15]	0.00	0.541	1.64E-01	0	0	0	0	TRIM40
26	6:30108683	rs9261484	t	c	0.2381	0.0220	DEPR	DEPR_surv	1314	0.112	0.091	1.12 [0.94, 1.34]	47.80	0.088	2.17E-01	0	0	0	0	TRIM40
27	6:30108683	rs9261484	t	c	0.2451	0.0270	INS	INS_base	2220	-0.076	0.080	0.93 [0.79, 1.09]	0.00	0.527	3.46E-01	0	0	0	0	TRIM40
28	6:30108683	rs9261484	t	c	0.2293	0.0143	MOTORFLUX	MOTORFLUX_surv	1709	-0.052	0.058	0.95 [0.85, 1.06]	0.00	0.679	3.67E-01	0	0	0	0	TRIM40
29	6:30108683	rs9261484	t	c	0.2439	0.0151	MOTORFLUX	MOTORFLUX_base	1803	0.084	0.094	1.09 [0.90, 1.31]	0.00	0.421	3.73E-01	0	0	0	0	TRIM40
30	6:30108683	rs9261484	t	c	0.2502	0.0346	UPDRS3_scaled	UPDRS3_scaled_cont	2446	-0.025	0.029	-0.03 [-0.08, 0.03]	0.00	0.621	3.81E-01	0	0	0	0	TRIM40
31	6:30108683	rs9261484	t	c	0.2371	0.0115	DYSKINESIAS	DYSKINESIAS_surv	1856	0.051	0.068	1.05 [0.92, 1.20]	0.00	0.836	4.57E-01	0	0	0	0	TRIM40
32	6:30108683	rs9261484	t	c	0.2515	0.0103	DYSKINESIAS	DYSKINESIAS_base	1232	-0.064	0.118	0.94 [0.74, 1.18]	0.00	0.915	5.90E-01	0	0	0	0	TRIM40
33	6:30108683	rs9261484	t	c	0.2356	0.0276	HY	HY_cont	3627	0.004	0.010	0.00 [-0.02, 0.02]	0.00	0.610	6.72E-01	0	0	0	0	TRIM40
34	6:30108683	rs9261484	t	c	0.2428	0.0285	HYPOSIMIA	HYPOSIMIA_base	1588	0.035	0.092	1.04 [0.87, 1.24]	0.00	0.937	6.99E-01	0	0	0	0	TRIM40
35	6:30108683	rs9261484	t	c	0.2397	0.0133	INS	INS_surv	1112	-0.025	0.074	0.98 [0.84, 1.13]	37.90	0.153	7.35E-01	0	0	0	0	TRIM40
36	6:30108683	rs9261484	t	c	0.2344	0.0140	CONST	CONST_base	1472	0.024	0.098	1.02 [0.85, 1.24]	0.00	0.649	8.09E-01	0	0	0	0	TRIM40
37	6:30108683	rs9261484	t	c	0.2305	0.0235	MMSE	MMSE_cont	2114	-0.011	0.052	-0.01 [-0.11, 0.09]	0.00	0.993	8.30E-01	0	0	0	0	TRIM40
38	6:30108683	rs9261484	t	c	0.2351	0.0167	DEPR	DEPR_base	2138	0.020	0.103	1.02 [0.83, 1.25]	2.60	0.410	8.49E-01	0	0	0	0	TRIM40
39	6:30108683	rs9261484	t	c	0.2449	0.0233	COGI	COGI_base	2859	-0.018	0.099	0.98 [0.81, 1.19]	0.00	0.964	8.53E-01	0	0	0	0	TRIM40
40	6:30108683	rs9261484	t	c	0.2414	0.0285	UPDRS2_scaled	UPDRS2_scaled_cont	2103	0.006	0.033	0.01 [-0.06, 0.07]	37.20	0.145	8.63E-01	0	0	0	0	TRIM40
41	6:30108683	rs9261484	t	c	0.2373	0.0285	UPDRS4_scaled	UPDRS4_scaled_cont	1798	-0.003	0.029	-0.00 [-0.06, 0.05]	15.90	0.311	9.04E-01	0	0	0	0	TRIM40
42	6:30108683	rs9261484	t	c	0.2431	0.0303	HY3	HY3_surv	2582	0.008	0.072	1.01 [0.87, 1.16]	11.70	0.337	9.13E-01	0	0	0	0	TRIM40
43	6:30108683	rs9261484	t	c	0.2384	0.0264	UPDRS_scaled	UPDRS_scaled_cont	2994	-0.001	0.027	-0.00 [-0.05, 0.05]	12.80	0.326	9.62E-01	0	0	0	0	TRIM40
44	10:15557406	rs896435	t	c	0.7000	0.0126	MOTORFLUX	MOTORFLUX_base	1803	0.172	0.089	1.19 [1.00, 1.41]	0.00	0.649	5.29E-02	0	0	0	0	ITGA8
45	10:15557406	rs896435	t	c	0.6981	0.0292	UPDRS4_scaled	UPDRS4_scaled_cont	1798	0.031	0.027	0.03 [-0.02, 0.08]	0.00	0.684	2.43E-01	0	0	0	0	ITGA8
46	10:15557406	rs896435	t	c	0.6970	0.0267	COGI	COGI_surv	2244	-0.087	0.078	0.92 [0.79, 1.07]	29.10	0.186	2.62E-01	0	0	0	0	ITGA8
47	10:15557406	rs896435	t	c	0.6950	0.0229	COGI	COGI_base	2859	0.101	0.093	1.11 [0.92, 1.33]	0.00	0.680	2.80E-01	0	0	0	0	ITGA8
48	10:15557406	rs896435	t	c	0.6940	0.0253	SLEEP	SLEEP_base	1724	-0.071	0.090	0.93 [0.78, 1.11]	0.00	0.444	4.30E-01	0	0	0	0	ITGA8
49	10:15557406	rs896435	t	c	0.6971	0.0296	UPDRS2_scaled	UPDRS2_scaled_cont	2103	-0.023	0.031	-0.02 [-0.08, 0.04]	36.70	0.149	4.65E-01	0	0	0	0	ITGA8
50	10:15557406	rs896435	t	c	0.6846	0.0196	SEADL	SEADL_cont	2218	0.179	0.248	1.18 [-0.31, 0.67]	0.00	0.936	4.71E-01	0	0	0	0	ITGA8
51	10:15557406	rs896435	t	c	0.7088	0.0163	HY3	HY3_base	1289	0.082	0.127	1.09 [0.85, 1.39]	0.00	0.795	5.15E-01	0	0	0	0	ITGA8
52	10:15557406	rs896435	t	c	0.6938	0.0258	UPDRS_scaled	UPDRS_scaled_cont	2994	-0.016	0.025	-0.02 [-0.06, 0.03]	44.50	0.063	5.29E-01	0	0	0	0	ITGA8
53	10:15557406	rs896435	t	c	0.6927	0.0277	UPDRS3_scaled	UPDRS3_scaled_cont	2446	-0.014	0.028	-0.01 [-0.07, 0.04]	48.60	0.058	6.26E-01	0	0	0	0	ITGA8
54	10:15557406	rs896435	t	c	0.6990	0.0169	MOTORFLUX	MOTORFLUX_surv	1709	0.022	0.053	1.02 [0.92, 1.13]	0.00	0.610	6.78E-01	0	0	0	0	ITGA8
55	10:15557406	rs896435	t	c	0.6904	0.0280	HYPOSIMIA	HYPOSIMIA_base	1588	0.032	0.086	1.03 [0.87, 1.22]	0.00	0.490	7.14E-01	0	0	0	0	ITGA8
56	10:15557406	rs896435	t	c	0.7064	0.0203	INS	INS_surv	1112	-0.027	0.074	0.97 [0.84, 1.13]	0.00	0.908	7.22E-01	0	0	0	0	ITGA8
57	10:15557406	rs896435	t	c	0.6949	0.0142	SEADL70	SEADL70_surv	1683	0.033	0.098	1.03 [0.85, 1.25]	0.00	0.674	7.35E-01	0	0	0	0	ITGA8
58	10:15557406	rs896435	t	c	0.7048	0.0201	DYSKINESIAS	DYSKINESIAS_surv	1856	0.019	0.062	1.02 [0.90, 1.15]	0.00	0.990	7.65E-01	0	0	0	0	ITGA8
59	10:15557406	rs896435	t	c	0.7000	0.0157	CONST	CONST_base	1472	-0.026	0.092	0.97 [0.81, 1.17]	0.00	0.895	7.74E-01	0	0	0	0	ITGA8
60	10:15557406	rs896435	t	c	0.6948	0.0156	DEPR	DEPR_base	2138	-0.026	0.099	0.97 [0.80, 1.18]	0.00	0.605	7.91E-01	0	0	0	0	ITGA8
61	10:15557406	rs896435	t	c	0.6914	0.0234	HY	HY_cont	3627	0.002	0.010	0.00								

1	20:6006041	rs77351827	t	c	0.1329	0.0083	UPDRS1_scaled	UPDRS1_scaled_cont	2111	0.062	0.043	0.06 [-0.02, 0.15]	0.00	0.449	1.50E-01	0	0	0	0	CRLS1
2	20:6006041	rs77351827	t	c	0.1300	0.0092	HYPOSIMIA	HYPOSIMIA_base	1588	-0.151	0.116	0.86 [0.68, 1.08]	34.90	0.175	1.92E-01	0	0	0	0	CRLS1
2	20:6006041	rs77351827	t	c	0.1315	0.0060	DEPR	DEPR_surv	1314	0.139	0.115	1.15 [0.92, 1.44]	38.20	0.152	2.28E-01	0	0	0	0	CRLS1
3	20:6006041	rs77351827	t	c	0.1313	0.0038	INS	INS_surv	1112	-0.117	0.100	0.89 [0.73, 1.08]	0.00	0.665	2.41E-01	0	0	0	0	CRLS1
3	20:6006041	rs77351827	t	c	0.1342	0.0085	COGi	COGi_surv	2712	0.119	0.122	1.13 [0.89, 1.43]	0.00	0.668	3.31E-01	0	0	0	0	CRLS1
4	20:6006041	rs77351827	t	c	0.1335	0.0085	UPDRS4_scaled	UPDRS4_scaled_cont	1798	-0.034	0.037	-0.03 [-0.11, 0.04]	38.30	0.151	3.59E-01	0	0	0	0	CRLS1
4	20:6006041	rs77351827	t	c	0.1311	0.0056	MOTORFLUX	MOTORFLUX_base	1803	-0.104	0.115	0.90 [0.72, 1.13]	0.00	0.439	3.67E-01	0	0	0	0	CRLS1
5	20:6006041	rs77351827	t	c	0.1330	0.0073	HY3	HY3_base	1289	0.139	0.157	1.15 [0.84, 1.56]	0.00	0.943	3.76E-01	0	0	0	0	CRLS1
5	20:6006041	rs77351827	t	c	0.1307	0.0073	MMSE	MMSE_cont	2114	-0.058	0.066	-0.06 [-0.19, 0.07]	0.00	0.765	3.81E-01	0	0	0	0	CRLS1
6	20:6006041	rs77351827	t	c	0.1315	0.0069	CONST	CONST_base	1472	0.105	0.121	1.11 [0.88, 1.41]	0.00	0.898	3.88E-01	0	0	0	0	CRLS1
6	20:6006041	rs77351827	t	c	0.1325	0.0095	UPDRS2_scaled	UPDRS2_scaled_cont	2103	0.035	0.043	0.03 [-0.05, 0.12]	15.50	0.311	4.16E-01	0	0	0	0	CRLS1
7	20:6006041	rs77351827	t	c	0.1303	0.0087	SLEEP	SLEEP_base	1724	0.097	0.121	1.10 [0.87, 1.40]	0.00	0.719	4.21E-01	0	0	0	0	CRLS1
7	20:6006041	rs77351827	t	c	0.1367	0.0094	MOTORFLUX	MOTORFLUX_surv	1709	0.048	0.071	1.05 [0.91, 1.21]	0.00	0.614	5.01E-01	0	0	0	0	CRLS1
8	20:6006041	rs77351827	t	c	0.1312	0.0071	INS	INS_base	2220	0.061	0.101	1.06 [0.87, 1.30]	38.40	0.124	5.48E-01	0	0	0	0	CRLS1
8	20:6006041	rs77351827	t	c	0.1299	0.0090	UPDRS3_scaled	UPDRS3_scaled_cont	2446	-0.023	0.039	-0.02 [-0.10, 0.05]	0.00	0.736	5.51E-01	0	0	0	0	CRLS1
9	20:6006041	rs77351827	t	c	0.1311	0.0059	DEPR	DEPR_base	2138	0.065	0.128	1.07 [0.83, 1.37]	13.30	0.326	6.11E-01	0	0	0	0	CRLS1
9	20:6006041	rs77351827	t	c	0.1317	0.0043	HY3	HY3_surv	2582	-0.028	0.096	0.97 [0.81, 1.17]	0.00	0.633	7.67E-01	0	0	0	0	CRLS1
10	20:6006041	rs77351827	t	c	0.1276	0.0081	SEADL	SEADL_cont	2218	0.105	0.356	0.11 [-0.59, 0.80]	5.60	0.387	7.67E-01	0	0	0	0	CRLS1
10	20:6006041	rs77351827	t	c	0.1325	0.0074	DYSKINESIAS	DYSKINESIAS_surv	1856	-0.023	0.085	0.98 [0.83, 1.16]	0.00	0.473	7.92E-01	0	0	0	0	CRLS1
11	20:6006041	rs77351827	t	c	0.1341	0.0055	MOCA	MOCA_cont	1074	0.040	0.180	0.04 [-0.31, 0.39]	17.90	0.301	8.25E-01	0	0	0	0	CRLS1
11	20:6006041	rs77351827	t	c	0.1318	0.0058	DYSKINESIAS	DYSKINESIAS_base	1232	0.025	0.143	1.03 [0.77, 1.36]	60.50	0.080	8.63E-01	0	0	0	0	CRLS1
12	20:6006041	rs77351827	t	c	0.1337	0.0100	UPDRS_scaled	UPDRS_scaled_cont	2994	0.005	0.035	0.00 [-0.06, 0.07]	0.00	0.909	8.97E-01	0	0	0	0	CRLS1
12	20:6006041	rs77351827	t	c	0.1334	0.0107	HY	HY_cont	3627	0.001	0.013	0.00 [-0.02, 0.03]	0.00	0.946	9.29E-01	0	0	0	0	CRLS1
13	20:6006041	rs77351827	t	c	0.1305	0.0072	COGi	COGi_surv	2244	0.005	0.118	1.00 [0.80, 1.27]	0.00	0.632	9.69E-01	0	0	0	0	CRLS1
14	8:16697593	rs620513	t	g	0.2631	0.0109	CONST	CONST_base	1472	0.187	0.100	1.21 [0.99, 1.47]	0.00	0.439	6.24E-02	0	0	0	0	FGF20
14	8:16697593	rs620513	t	g	0.2637	0.0053	HY3	HY3_base	1289	0.219	0.137	1.24 [0.95, 1.63]	0.00	0.460	1.11E-01	0	0	0	0	FGF20
14	8:16697593	rs620513	t	g	0.2524	0.0203	HY3	HY3_surv	2582	-0.093	0.074	0.91 [0.79, 1.05]	17.00	0.291	2.10E-01	0	0	0	0	FGF20
15	8:16697593	rs620513	t	g	0.2550	0.0201	COGi	COGi_surv	2244	0.101	0.086	1.11 [0.93, 1.31]	0.00	0.576	2.41E-01	0	0	0	0	FGF20
15	8:16697593	rs620513	t	g	0.2583	0.0131	DEPR	DEPR_base	2138	0.101	0.104	1.11 [0.90, 1.36]	0.00	0.679	3.34E-01	0	0	0	0	FGF20
16	8:16697593	rs620513	t	g	0.2393	0.0148	UPDRS2_scaled	UPDRS2_scaled_cont	2103	0.030	0.034	0.03 [-0.04, 0.10]	49.30	0.066	3.75E-01	0	0	0	0	FGF20
16	8:16697593	rs620513	t	g	0.2609	0.0121	SLEEP	SLEEP_base	1724	0.078	0.098	1.08 [0.89, 1.31]	0.00	0.958	4.25E-01	0	0	0	0	FGF20
17	8:16697593	rs620513	t	g	0.2482	0.0117	SEADL	SEADL_cont	2112	0.174	0.270	0.17 [-0.36, 0.70]	0.00	0.517	5.19E-01	0	0	0	0	FGF20
17	8:16697593	rs620513	t	g	0.2376	0.0133	UPDRS4_scaled	UPDRS4_scaled_cont	1798	-0.019	0.030	-0.02 [-0.08, 0.04]	0.00	0.721	5.22E-01	0	0	0	0	FGF20
18	8:16697593	rs620513	t	g	0.2397	0.0143	UPDRS3_scaled	UPDRS3_scaled_cont	2446	-0.018	0.030	-0.02 [-0.08, 0.04]	2.60	0.410	5.49E-01	0	0	0	0	FGF20
18	8:16697593	rs620513	t	g	0.2604	0.0088	HYPOSIMIA	HYPOSIMIA_base	1588	-0.057	0.096	0.94 [0.78, 1.14]	33.90	0.182	5.51E-01	0	0	0	0	FGF20
19	8:16697593	rs620513	t	g	0.2463	0.0151	MOTORFLUX	MOTORFLUX_surv	1709	0.034	0.059	1.03 [0.92, 1.16]	0.00	0.587	5.62E-01	0	0	0	0	FGF20
19	8:16697593	rs620513	t	g	0.2501	0.0127	DYSKINESIAS	DYSKINESIAS_surv	1856	0.040	0.070	1.04 [0.91, 1.19]	25.60	0.234	5.70E-01	0	0	0	0	FGF20
20	8:16697593	rs620513	t	g	0.2627	0.0111	INS	INS_base	2220	0.047	0.083	1.05 [0.89, 1.23]	4.10	0.399	5.73E-01	0	0	0	0	FGF20
20	8:16697593	rs620513	t	g	0.2397	0.0139	UPDRS1_scaled	UPDRS1_scaled_cont	2111	0.019	0.034	0.02 [-0.05, 0.09]	17.30	0.298	5.77E-01	0	0	0	0	FGF20
21	8:16697593	rs620513	t	g	0.2634	0.0374	INS	INS_surv	1112	0.014	0.077	1.01 [0.87, 1.18]	0.00	0.733	8.55E-01	0	0	0	0	FGF20
21	8:16697593	rs620513	t	g	0.2453	0.0129	DEPR	DEPR_surv	1314	0.016	0.089	1.02 [0.85, 1.21]	9.40	0.356	8.55E-01	0	0	0	0	FGF20
22	8:16697593	rs620513	t	g	0.2582	0.0087	MOTORFLUX	MOTORFLUX_base	1803	0.013	0.096	1.01 [0.84, 1.22]	0.00	0.618	8.90E-01	0	0	0	0	FGF20
22	8:16697593	rs620513	t	g	0.2471	0.0223	UPDRS_scaled	UPDRS_scaled_cont	2994	0.002	0.027	0.00 [-0.05, 0.05]	0.00	0.494	9.54E-01	0	0	0	0	FGF20
23	8:16697593	rs620513	t	g	0.2495	0.0148	SEADL70	SEADL70_surv	1683	0.006	0.110	1.01 [0.81, 1.25]	0.00	0.408	9.56E-01	0	0	0	0	FGF20
23	8:16697593	rs620513	t	g	0.2497	0.0187	HY	HY_cont	3627	0.000	0.010	0.00 [-0.02, 0.02]	11.60	0.331	9.79E-01	0	0	0	0	FGF20
24	17:43798308	rs117615688	a	g	0.0484	0.0073	HY3	HY3_base	1289	-0.605	0.330	0.55 [0.29, 1.04]	0.00	0.751	6.69E-02	0	0	0	0	CRHR1
24	17:43798308	rs117615688	a	g	0.0510	0.0062	COGi	COGi_base	2450	0.340	0.200	1.40 [0.95, 2.08]	10.10	0.352	8.92E-02	0	0	0	0	CRHR1
25	17:43798308	rs117615688	a	g	0.0540	0.0090	CONST	CONST_base	1355	-0.341	0.211	0.71 [0.47, 1.08]	0.00	0.788	1.07E-01	0	0	0	0	CRHR1
25	17:43798308	rs117615688	a	g	0.0497	0.0052	SEADL	SEADL_cont	2218	0.891	0.563	0.89 [-0.21, 2.00]	0.00	0.726	1.14E-01	0	0	0	0	CRHR1
26	17:43798308	rs117615688	a	g	0.0557	0.0146	SLEEP	SLEEP_base	1724	0.309	0.196	1.36 [0.93, 2.00]	10.70	0.348	1.15E-01	0	0	0	0	CRHR1
26	17:43798308	rs117615688	a	g	0.0503	0.0031	DEPR	DEPR_surv	1314	0.276	0.179	1.32 [0.93, 1.87]	21.80	0.270	1.22E-01	0	0	0	0	CRHR1
27	17:43798308	rs117615688	a	g	0.0584	0.0140	HYPOSIMIA	HYPOSIMIA_base	1588	0.247	0.186	1.28 [0.89, 1.84]	54.40	0.052	1.84E-01	0	0	0	0	CRHR1
27	17:43798308	rs117615688	a	g	0.0517	0.0089	MOTORFLUX	MOTORFLUX_surv	1709	-0.123	0.122	0.88 [0.70, 1.12]	0.00	0.658	3.13E-01	0	0	0	0	CRHR1
28	17:43798308	rs117615688	a	g	0.0519	0.0049	MOTORFLUX	MOTORFLUX_base	1803	0.188	0.199	1.21 [0.82, 1.78]	16.70	0.308	3.43E-01	0	0	0	0	CRHR1
28	17:43798308	rs117615688	a	g	0.0597	0.0128	INS	INS_base	2220	0.154	0.173	1.17 [0.83, 1.64]	41.50	0.102	3.74E-01	0	0	0	0	CRHR1
29	17:43798308	rs117615688	a	g	0.0519	0.0126	UPDRS4_scaled	UPDRS4_scaled_cont	1798	-0.053	0.061	-0.05 [-0.17, 0.07]	2.90	0.398	3.80E-01	0	0	0	0	CRHR1
29	17:43798308	rs117615688	a	g	0.0524	0.0140	HY	HY_cont	3627	0.017	0.021	0.02 [-0.02, 0.06]	14.40	0.304	4.23E-01	0	0	0	0	CRHR1
30	17:43798308	rs117615688	a	g	0.0548	0.0079	INS	INS_surv	1112	0.107	0.152	1.11 [0.83, 1.50]	0.00	0.672	4.83E-01	0	0	0	0	CRHR1
30	17:43798308	rs117615688	a	g	0.0501	0.0150	UPDRS3_scaled	UPDRS3_scaled_cont	2446	0.038	0.066	0.04 [-0.09, 0.17]	0.00	0.772	5.59E-01	0	0	0	0	CRHR1
31	17:43798308	rs117615688	a	g	0.0522	0.0133	UPDRS1_scaled	UPDRS1_scaled_cont	2111	0.036	0.070	0.04 [-0.10, 0.17]	0.00	0.637	6.09E-01	0	0	0	0	CRHR1
31	17:43798308	rs117615688	a	g	0.0510	0.0124	UPDRS_scaled	UPDRS_scaled_cont	2994	-0.028	0.057	-0								

1	10:121415685	rs72840788	a	g	0.2287	0.0106	DYSKINESIAS	DYSKINESIAS_base	1232	-0.057	0.119	0.94 [0.75, 1.19]	59.70	0.084	6.34E-01	0	0	0	0	BAG3
2	10:121415685	rs72840788	a	g	0.2307	0.0105	UPDRS1_scaled	UPDRS1_scaled_cont	2111	-0.016	0.034	-0.02 [-0.08, 0.05]	0.00	0.693	6.44E-01	0	0	0	0	BAG3
3	10:121415685	rs72840788	a	g	0.2328	0.0135	SLEEP	SLEEP_base	1724	-0.032	0.097	0.97 [0.80, 1.17]	0.00	0.920	7.38E-01	0	0	0	0	BAG3
4	10:121415685	rs72840788	a	g	0.2243	0.0144	SEADL	SEADL_cont	2218	-0.084	0.275	-0.08 [-0.62, 0.45]	6.60	0.379	7.59E-01	0	0	0	0	BAG3
5	10:121415685	rs72840788	a	g	0.2314	0.0120	CONST	CONST_base	1472	0.028	0.100	1.03 [0.84, 1.25]	10.80	0.344	7.82E-01	0	0	0	0	BAG3
6	10:121415685	rs72840788	a	g	0.2292	0.0160	DYSKINESIAS	DYSKINESIAS_surv	1856	-0.016	0.068	0.98 [0.86, 1.13]	11.40	0.343	8.15E-01	0	0	0	0	BAG3
7	10:121415685	rs72840788	a	g	0.2153	0.0140	MMSE	MMSE_cont	2114	-0.010	0.053	-0.01 [-0.11, 0.10]	0.00	0.875	8.59E-01	0	0	0	0	BAG3
8	10:121415685	rs72840788	a	g	0.2346	0.0212	HY3	HY3_surv	2582	-0.012	0.072	0.99 [0.86, 1.14]	31.70	0.165	8.71E-01	0	0	0	0	BAG3
9	10:121415685	rs72840788	a	g	0.2306	0.0139	COGI	COGI_base	2859	0.013	0.102	1.01 [0.83, 1.24]	17.60	0.291	8.96E-01	0	0	0	0	BAG3
10	10:121415685	rs72840788	a	g	0.2279	0.0133	UPDRS_scaled	UPDRS_scaled_cont	2994	-0.002	0.028	-0.00 [-0.06, 0.05]	0.00	0.762	9.36E-01	0	0	0	0	BAG3
11	10:121415685	rs72840788	a	g	0.2285	0.0139	INS	INS_base	2220	0.000	0.084	1.00 [0.85, 1.18]	26.30	0.219	9.97E-01	0	0	0	0	BAG3
12	17:7355621	rs12600861	a	c	0.6426	0.0238	SEADL	SEADL_cont	2218	-0.429	0.244	-0.43 [-0.91, 0.05]	0.90	0.423	7.91E-02	0	0	0	0	CHRNBI
13	17:7355621	rs12600861	a	c	0.6329	0.0298	HY	HY_cont	3627	0.013	0.009	0.01 [-0.00, 0.03]	0.00	0.637	1.42E-01	0	0	0	0	CHRNBI
14	17:7355621	rs12600861	a	c	0.6479	0.0185	MOCA	MOCA_cont	1074	-0.179	0.124	-0.18 [-0.42, 0.06]	23.40	0.271	1.50E-01	0	0	0	0	CHRNBI
15	17:7355621	rs12600861	a	c	0.6359	0.0299	UPDRS_scaled	UPDRS_scaled_cont	2994	0.034	0.024	0.03 [-0.01, 0.08]	0.00	0.739	1.54E-01	0	0	0	0	CHRNBI
16	17:7355621	rs12600861	a	c	0.6452	0.0141	DYSKINESIAS	DYSKINESIAS_base	1232	0.108	0.105	1.11 [0.91, 1.37]	46.80	0.153	3.07E-01	0	0	0	0	CHRNBI
17	17:7355621	rs12600861	a	c	0.6417	0.0211	UPDRS1_scaled	UPDRS1_scaled_cont	2111	0.028	0.030	0.03 [-0.03, 0.09]	38.40	0.136	3.45E-01	0	0	0	0	CHRNBI
18	17:7355621	rs12600861	a	c	0.6383	0.0178	HY3	HY3_base	1289	-0.085	0.117	0.92 [0.73, 1.16]	0.00	0.444	4.71E-01	0	0	0	0	CHRNBI
19	17:7355621	rs12600861	a	c	0.6409	0.0144	MOTORFLUX	MOTORFLUX_base	1803	-0.059	0.084	0.94 [0.80, 1.11]	0.00	0.458	4.81E-01	0	0	0	0	CHRNBI
20	17:7355621	rs12600861	a	c	0.6411	0.0185	DYSKINESIAS	DYSKINESIAS_surv	1856	0.041	0.059	1.04 [0.93, 1.17]	28.00	0.215	4.87E-01	0	0	0	0	CHRNBI
21	17:7355621	rs12600861	a	c	0.6402	0.0220	HY3	HY3_surv	2582	-0.039	0.064	0.96 [0.85, 1.09]	13.80	0.320	5.47E-01	0	0	0	0	CHRNBI
22	17:7355621	rs12600861	a	c	0.6420	0.0258	SLEEP	SLEEP_base	1724	0.050	0.085	1.05 [0.89, 1.24]	0.00	0.999	5.62E-01	0	0	0	0	CHRNBI
23	17:7355621	rs12600861	a	c	0.6380	0.0254	DEPR	DEPR_surv	1314	0.045	0.079	1.05 [0.90, 1.22]	0.00	0.800	5.69E-01	0	0	0	0	CHRNBI
24	17:7355621	rs12600861	a	c	0.6461	0.0196	CONST	CONST_base	1472	-0.049	0.087	0.95 [0.80, 1.13]	0.00	0.485	5.75E-01	0	0	0	0	CHRNBI
25	17:7355621	rs12600861	a	c	0.6499	0.0177	MOTORFLUX	MOTORFLUX_surv	1709	0.027	0.051	1.03 [0.93, 1.14]	0.00	0.713	5.91E-01	0	0	0	0	CHRNBI
26	17:7355621	rs12600861	a	c	0.6531	0.0217	MMSE	MMSE_cont	2114	-0.023	0.047	-0.02 [-0.11, 0.07]	0.00	0.524	6.18E-01	0	0	0	0	CHRNBI
27	17:7355621	rs12600861	a	c	0.6333	0.0311	COGI	COGI_base	2859	-0.036	0.089	0.96 [0.81, 1.15]	41.00	0.105	6.84E-01	0	0	0	0	CHRNBI
28	17:7355621	rs12600861	a	c	0.6415	0.0213	UPDRS2_scaled	UPDRS2_scaled_cont	2103	0.012	0.030	0.01 [-0.05, 0.07]	0.00	0.540	6.91E-01	0	0	0	0	CHRNBI
29	17:7355621	rs12600861	a	c	0.6374	0.0223	UPDRS3_scaled	UPDRS3_scaled_cont	2446	-0.008	0.027	-0.01 [-0.06, 0.04]	0.00	0.916	7.52E-01	0	0	0	0	CHRNBI
30	17:7355621	rs12600861	a	c	0.6518	0.0207	COGI	COGI_surv	2244	-0.023	0.076	0.98 [0.84, 1.14]	0.00	0.672	7.67E-01	0	0	0	0	CHRNBI
31	17:7355621	rs12600861	a	c	0.6570	0.0167	SEADL70	SEADL70_surv	1683	-0.026	0.096	0.97 [0.81, 1.18]	0.00	0.910	7.88E-01	0	0	0	0	CHRNBI
32	17:7355621	rs12600861	a	c	0.6437	0.0183	DEPR	DEPR_base	2138	0.022	0.093	1.02 [0.85, 1.23]	16.40	0.301	8.10E-01	0	0	0	0	CHRNBI
33	17:7355621	rs12600861	a	c	0.6425	0.0279	HYPOSIMIA	HYPOSIMIA_base	1588	-0.013	0.083	0.99 [0.84, 1.16]	0.00	0.897	8.71E-01	0	0	0	0	CHRNBI
34	17:7355621	rs12600861	a	c	0.6443	0.0237	INS	INS_base	2220	0.003	0.072	1.00 [0.87, 1.16]	0.00	0.639	9.63E-01	0	0	0	0	CHRNBI
35	17:7355621	rs12600861	a	c	0.6558	0.0200	INS	INS_surv	1112	0.001	0.067	1.00 [0.88, 1.14]	0.00	0.780	9.87E-01	0	0	0	0	CHRNBI
36	16:30977799	rs11150601	a	g	0.6731	0.0194	INS	INS_surv	1112	-0.123	0.071	0.88 [0.77, 1.01]	46.40	0.097	8.01E-02	0	0	0	0	SETDIA
37	16:30977799	rs11150601	a	g	0.6503	0.0272	HY3	HY3_surv	2582	-0.105	0.064	0.90 [0.79, 1.02]	0.00	0.899	1.02E-01	0	0	0	0	SETDIA
38	16:30977799	rs11150601	a	g	0.6542	0.0186	UPDRS2_scaled	UPDRS2_scaled_cont	2103	-0.049	0.030	-0.05 [-0.11, 0.01]	0.00	0.750	1.06E-01	0	0	0	0	SETDIA
39	16:30977799	rs11150601	a	g	0.6540	0.0263	INS	INS_base	2220	-0.119	0.074	0.89 [0.77, 1.03]	25.10	0.229	1.07E-01	0	0	0	0	SETDIA
40	16:30977799	rs11150601	a	g	0.6536	0.0190	UPDRS1_scaled	UPDRS1_scaled_cont	2111	-0.046	0.030	-0.05 [-0.11, 0.01]	0.00	0.954	1.29E-01	0	0	0	0	SETDIA
41	16:30977799	rs11150601	a	g	0.6544	0.0231	HY	HY_cont	3627	-0.012	0.009	-0.01 [-0.03, 0.01]	15.80	0.289	1.86E-01	0	0	0	0	SETDIA
42	16:30977799	rs11150601	a	g	0.6603	0.0188	HYPOSIMIA	HYPOSIMIA_base	1588	-0.110	0.084	0.90 [0.76, 1.06]	0.00	0.953	1.88E-01	0	0	0	0	SETDIA
43	16:30977799	rs11150601	a	g	0.6439	0.0144	SEADL70	SEADL70_surv	1683	0.118	0.098	1.12 [0.93, 1.36]	0.00	0.925	2.27E-01	0	0	0	0	SETDIA
44	16:30977799	rs11150601	a	g	0.6518	0.0169	COGI	COGI_base	2859	0.106	0.092	1.11 [0.93, 1.33]	40.00	0.112	2.49E-01	0	0	0	0	SETDIA
45	16:30977799	rs11150601	a	g	0.6534	0.0203	UPDRS4_scaled	UPDRS4_scaled_cont	1798	-0.026	0.026	-0.03 [-0.08, 0.03]	0.00	0.828	3.25E-01	0	0	0	0	SETDIA
46	16:30977799	rs11150601	a	g	0.6480	0.0151	MOTORFLUX	MOTORFLUX_base	1803	0.083	0.086	1.09 [0.92, 1.29]	0.00	0.836	3.38E-01	0	0	0	0	SETDIA
47	16:30977799	rs11150601	a	g	0.6571	0.0185	DEPR	DEPR_surv	1314	-0.069	0.080	0.93 [0.80, 1.09]	4.90	0.385	3.85E-01	0	0	0	0	SETDIA
48	16:30977799	rs11150601	a	g	0.6476	0.0259	UPDRS_scaled	UPDRS_scaled_cont	2994	-0.021	0.025	-0.02 [-0.07, 0.03]	0.00	0.935	3.85E-01	0	0	0	0	SETDIA
49	16:30977799	rs11150601	a	g	0.6526	0.0287	SLEEP	SLEEP_base	1724	-0.075	0.087	0.93 [0.78, 1.10]	22.70	0.256	3.86E-01	0	0	0	0	SETDIA
50	16:30977799	rs11150601	a	g	0.6451	0.0287	DEPR	DEPR_base	2138	-0.057	0.093	0.94 [0.79, 1.13]	0.00	0.565	5.38E-01	0	0	0	0	SETDIA
51	16:30977799	rs11150601	a	g	0.6544	0.0148	HY3	HY3_base	1289	0.063	0.122	1.07 [0.84, 1.35]	0.00	0.840	6.04E-01	0	0	0	0	SETDIA
52	16:30977799	rs11150601	a	g	0.6534	0.0268	MMSE	MMSE_cont	2114	0.024	0.046	0.02 [-0.07, 0.11]	0.00	0.964	6.06E-01	0	0	0	0	SETDIA
53	16:30977799	rs11150601	a	g	0.6483	0.0175	MOTORFLUX	MOTORFLUX_surv	1709	0.019	0.051	1.02 [0.92, 1.13]	47.20	0.078	7.06E-01	0	0	0	0	SETDIA
54	16:30977799	rs11150601	a	g	0.6521	0.0273	CONST	CONST_base	1472	-0.029	0.090	0.97 [0.81, 1.16]	0.00	0.435	7.45E-01	0	0	0	0	SETDIA
55	16:30977799	rs11150601	a	g	0.6556	0.0184	UPDRS3_scaled	UPDRS3_scaled_cont	2446	-0.009	0.027	-0.01 [-0.06, 0.04]	0.00	0.769	7.54E-01	0	0	0	0	SETDIA
56	16:30977799	rs11150601	a	g	0.6520	0.0154	SEADL	SEADL_cont	2218	0.068	0.243	0.07 [-0.41, 0.54]	0.00	0.707	7.79E-01	0	0	0	0	SETDIA
57	16:30977799	rs11150601	a	g	0.6484	0.0101	MOCA	MOCA_cont	1074	0.025	0.126	0.03 [-0.22, 0.27]	43.20	0.152	8.41E-01	0	0	0	0	SETDIA
58	16:30977799	rs11150601	a	g	0.6567	0.0255	DYSKINESIAS	DYSKINESIAS_surv	1856	-0.010	0.060	0.99 [0.88, 1.11]	47.70	0.075	8.68E-01	0	0	0	0	SETDIA
59	16:30977799	rs11150601	a	g	0.6503	0.0139	DYSKINESIAS	DYSKINESIAS_base	1232	-0.011	0.108	0.99 [0.80, 1.22]	66.30	0.052	9.20E-01	0	0	0	0	SETDIA
60	15:61997385	rs2251086	t	c	0.1288	0.0007	DYSKINESIAS	DYSKINESIAS_base	1232	-0.276	0.158	0.76 [0.56, 1.03]	0.00	0.661	8.12E-02	0	0	0	0	VPSI3C
61	15:61997385	rs225																		

1	9:34046391	rs6476434	t	c	0.7220	0.0156	INS	INS_surv	1112	-0.084	0.072	0.92	[0.80, 1.06]	0.00	0.809	2.45E-01	0	0	0	0	UBAP2
2	9:34046391	rs6476434	t	c	0.7275	0.0110	CONST	CONST_base	1472	0.105	0.095	1.11	[0.92, 1.34]	0.00	0.467	2.67E-01	0	0	0	0	UBAP2
3	9:34046391	rs6476434	t	c	0.7321	0.0081	HY3	HY3_base	1289	-0.119	0.129	0.89	[0.69, 1.14]	0.00	0.415	3.55E-01	0	0	0	0	UBAP2
4	9:34046391	rs6476434	t	c	0.7080	0.0143	MOCA	MOCA_cont	1074	0.119	0.134	0.12	[-0.14, 0.38]	0.00	0.805	3.77E-01	0	0	0	0	UBAP2
5	9:34046391	rs6476434	t	c	0.7234	0.0183	HY3	HY3_surv	2582	-0.059	0.071	0.94	[0.82, 1.08]	0.00	0.905	4.02E-01	0	0	0	0	UBAP2
6	9:34046391	rs6476434	t	c	0.7166	0.0152	HY	HY_cont	3627	0.007	0.010	0.01	[-0.01, 0.03]	25.10	0.197	4.58E-01	0	0	0	0	UBAP2
7	9:34046391	rs6476434	t	c	0.7270	0.0101	HYPOSMIA	HYPOSMIA_base	1588	0.062	0.091	1.06	[0.89, 1.27]	2.10	0.403	4.95E-01	0	0	0	0	UBAP2
8	9:34046391	rs6476434	t	c	0.7252	0.0094	INS	INS_base	2220	0.050	0.078	1.05	[0.90, 1.23]	0.00	0.501	5.20E-01	0	0	0	0	UBAP2
9	9:34046391	rs6476434	t	c	0.7097	0.0121	SEADL70	SEADL70_surv	1683	0.053	0.106	1.05	[0.86, 1.30]	0.00	0.510	6.14E-01	0	0	0	0	UBAP2
10	9:34046391	rs6476434	t	c	0.7101	0.0152	MMSE	MMSE_cont	2114	0.020	0.048	0.02	[-0.07, 0.11]	15.60	0.307	6.77E-01	0	0	0	0	UBAP2
11	9:34046391	rs6476434	t	c	0.7285	0.0100	SLEEP	SLEEP_base	1724	0.036	0.094	1.04	[0.86, 1.25]	27.40	0.220	6.99E-01	0	0	0	0	UBAP2
12	9:34046391	rs6476434	t	c	0.7132	0.0145	COGi	COGi_surv	2244	0.032	0.084	1.03	[0.88, 1.22]	2.90	0.410	7.08E-01	0	0	0	0	UBAP2
13	9:34046391	rs6476434	t	c	0.7277	0.0076	MOTORFLUX	MOTORFLUX_base	1803	-0.031	0.092	0.97	[0.81, 1.16]	0.00	0.417	7.32E-01	0	0	0	0	UBAP2
14	9:34046391	rs6476434	t	c	0.7070	0.0110	SEADL	SEADL_cont	2218	0.050	0.258	0.05	[-0.46, 0.56]	20.00	0.271	8.47E-01	0	0	0	0	UBAP2
15	9:34046391	rs6476434	t	c	0.7219	0.0175	DEPR	DEPR_surv	1314	0.014	0.090	1.01	[0.85, 1.21]	0.00	0.741	8.76E-01	0	0	0	0	UBAP2
16	9:34046391	rs6476434	t	c	0.7223	0.0060	UPDRS4_scaled	UPDRS4_scaled_cont	1798	0.003	0.028	0.00	[-0.05, 0.06]	43.30	0.116	9.09E-01	0	0	0	0	UBAP2
17	6:32578772	rs112485576	a	c	0.1439	0.0185	UPDRS1_scaled	UPDRS1_scaled_cont	2111	0.070	0.040	0.07	[-0.01, 0.15]	8.10	0.367	8.23E-02	0	0	0	0	HLA-DRB5
18	6:32578772	rs112485576	a	c	0.1450	0.0185	UPDRS2_scaled	UPDRS2_scaled_cont	2103	0.062	0.040	0.06	[-0.02, 0.14]	0.00	0.743	1.23E-01	0	0	0	0	HLA-DRB5
19	6:32578772	rs112485576	a	c	0.1436	0.0185	UPDRS3_scaled	UPDRS3_scaled_cont	2994	0.049	0.033	0.05	[-0.02, 0.11]	0.00	0.889	1.33E-01	0	0	0	0	HLA-DRB5
20	6:32578772	rs112485576	a	c	0.1484	0.0183	INS	INS_base	2220	-0.136	0.099	0.87	[0.72, 1.06]	0.00	0.548	1.72E-01	0	0	0	0	HLA-DRB5
21	6:32578772	rs112485576	a	c	0.1455	0.0182	UPDRS4_scaled	UPDRS4_scaled_cont	1798	0.045	0.035	0.04	[-0.02, 0.11]	0.00	0.851	2.00E-01	0	0	0	0	HLA-DRB5
22	6:32578772	rs112485576	a	c	0.1444	0.0161	DEPR	DEPR_base	2138	0.135	0.125	1.14	[0.90, 1.46]	0.00	0.878	2.80E-01	0	0	0	0	HLA-DRB5
23	6:32578772	rs112485576	a	c	0.1432	0.0174	COGi	COGi_surv	2244	0.106	0.104	1.11	[0.91, 1.36]	37.50	0.119	3.09E-01	0	0	0	0	HLA-DRB5
24	6:32578772	rs112485576	a	c	0.1514	0.0100	MOTORFLUX	MOTORFLUX_base	1803	-0.104	0.113	0.90	[0.72, 1.12]	0.00	0.687	3.57E-01	0	0	0	0	HLA-DRB5
25	6:32578772	rs112485576	a	c	0.1495	0.0141	COGi	COGi_base	2859	-0.106	0.124	0.90	[0.71, 1.15]	0.00	0.736	3.92E-01	0	0	0	0	HLA-DRB5
26	6:32578772	rs112485576	a	c	0.1421	0.0080	MOTORFLUX	MOTORFLUX_surv	1709	0.049	0.071	1.05	[0.91, 1.21]	0.00	0.575	4.86E-01	0	0	0	0	HLA-DRB5
27	6:32578772	rs112485576	a	c	0.1380	0.0027	HY	HY_cont	3627	-0.007	0.013	-0.01	[-0.03, 0.02]	0.00	0.901	5.78E-01	0	0	0	0	HLA-DRB5
28	6:32578772	rs112485576	a	c	0.1487	0.0108	HY3	HY3_base	1289	0.080	0.159	1.08	[0.79, 1.48]	28.00	0.249	6.17E-01	0	0	0	0	HLA-DRB5
29	6:32578772	rs112485576	a	c	0.1405	0.0099	DYSKINESIAS	DYSKINESIAS_surv	1856	-0.039	0.084	0.96	[0.82, 1.13]	0.00	0.603	6.47E-01	0	0	0	0	HLA-DRB5
30	6:32578772	rs112485576	a	c	0.1453	0.0209	HYPOSMIA	HYPOSMIA_base	1588	0.052	0.115	1.05	[0.84, 1.32]	0.00	0.768	6.51E-01	0	0	0	0	HLA-DRB5
31	6:32578772	rs112485576	a	c	0.1454	0.0201	SLEEP	SLEEP_base	1724	0.044	0.120	1.04	[0.83, 1.32]	19.50	0.281	7.16E-01	0	0	0	0	HLA-DRB5
32	6:32578772	rs112485576	a	c	0.1412	0.0244	SEADL	SEADL_cont	2218	0.119	0.337	0.12	[-0.54, 0.78]	0.00	0.970	7.23E-01	0	0	0	0	HLA-DRB5
33	6:32578772	rs112485576	a	c	0.1408	0.0151	MMSE	MMSE_cont	2114	-0.020	0.063	-0.02	[-0.14, 0.10]	0.00	0.768	7.55E-01	0	0	0	0	HLA-DRB5
34	6:32578772	rs112485576	a	c	0.1417	0.0070	SEADL70	SEADL70_surv	1683	0.031	0.128	1.03	[0.80, 1.33]	33.90	0.195	8.07E-01	0	0	0	0	HLA-DRB5
35	6:32578772	rs112485576	a	c	0.1406	0.0131	INS	INS_surv	1112	0.022	0.095	1.02	[0.85, 1.23]	0.00	0.912	8.18E-01	0	0	0	0	HLA-DRB5
36	6:32578772	rs112485576	a	c	0.1488	0.0160	HY3	HY3_surv	2582	0.019	0.086	1.02	[0.86, 1.21]	0.00	0.647	8.23E-01	0	0	0	0	HLA-DRB5
37	6:32578772	rs112485576	a	c	0.1338	0.0269	MOCA	MOCA_cont	1074	0.029	0.174	0.03	[-0.31, 0.37]	3.20	0.377	8.68E-01	0	0	0	0	HLA-DRB5
38	6:32578772	rs112485576	a	c	0.1489	0.0197	UPDRS3_scaled	UPDRS3_scaled_cont	2446	0.005	0.036	0.00	[-0.06, 0.07]	20.00	0.271	8.90E-01	0	0	0	0	HLA-DRB5
39	6:32578772	rs112485576	a	c	0.1443	0.0143	CONST	CONST_base	1472	0.015	0.121	1.02	[0.80, 1.29]	0.00	0.781	9.02E-01	0	0	0	0	HLA-DRB5
40	6:32578772	rs112485576	a	c	0.1372	0.0082	DEPR	DEPR_surv	1314	0.000	0.113	1.00	[0.80, 1.25]	0.00	0.904	9.98E-01	0	0	0	0	HLA-DRB5
41	10:104015279	rs10748818	a	g	0.8586	0.0126	DEPR	DEPR_base	2138	0.232	0.134	1.26	[0.97, 1.64]	0.00	0.987	8.39E-02	0	0	0	0	GBF1
42	10:104015279	rs10748818	a	g	0.8543	0.0115	HY3	HY3_surv	2582	-0.145	0.085	0.87	[0.73, 1.02]	0.00	0.511	8.88E-02	0	0	0	0	GBF1
43	10:104015279	rs10748818	a	g	0.8454	0.0163	DYSKINESIAS	DYSKINESIAS_base	1232	0.223	0.143	1.25	[0.94, 1.66]	0.00	0.732	1.19E-01	0	0	0	0	GBF1
44	10:104015279	rs10748818	a	g	0.8517	0.0197	UPDRS2_scaled	UPDRS2_scaled_cont	2103	0.053	0.041	0.05	[-0.03, 0.13]	0.00	0.826	1.87E-01	0	0	0	0	GBF1
45	10:104015279	rs10748818	a	g	0.8500	0.0173	DYSKINESIAS	DYSKINESIAS_surv	1856	0.108	0.083	1.11	[0.95, 1.31]	43.10	0.103	1.93E-01	0	0	0	0	GBF1
46	10:104015279	rs10748818	a	g	0.8530	0.0158	HY	HY_cont	3627	0.016	0.012	0.02	[-0.01, 0.04]	0.00	0.555	1.94E-01	0	0	0	0	GBF1
47	10:104015279	rs10748818	a	g	0.8623	0.0100	SLEEP	SLEEP_base	1724	0.157	0.123	1.17	[0.92, 1.49]	26.20	0.228	2.01E-01	0	0	0	0	GBF1
48	10:104015279	rs10748818	a	g	0.8488	0.0213	UPDRS3_scaled	UPDRS3_scaled_cont	2446	0.037	0.036	0.04	[-0.03, 0.11]	13.60	0.324	2.98E-01	0	0	0	0	GBF1
49	10:104015279	rs10748818	a	g	0.8468	0.0235	MOCA	MOCA_cont	1074	0.161	0.166	0.16	[-0.16, 0.49]	23.20	0.272	3.31E-01	0	0	0	0	GBF1
50	10:104015279	rs10748818	a	g	0.8550	0.0068	SEADL70	SEADL70_surv	1683	-0.117	0.123	0.89	[0.70, 1.13]	23.50	0.264	3.41E-01	0	0	0	0	GBF1
51	10:104015279	rs10748818	a	g	0.8500	0.0191	UPDRS4_scaled	UPDRS4_scaled_cont	1798	0.032	0.035	0.03	[-0.04, 0.10]	8.10	0.365	3.67E-01	0	0	0	0	GBF1
52	10:104015279	rs10748818	a	g	0.8531	0.0185	UPDRS1_scaled	UPDRS1_scaled_cont	2111	0.035	0.041	0.04	[-0.04, 0.11]	7.40	0.372	3.87E-01	0	0	0	0	GBF1
53	10:104015279	rs10748818	a	g	0.8515	0.0147	COGi	COGi_surv	2244	-0.085	0.104	0.92	[0.75, 1.13]	0.00	0.873	4.18E-01	0	0	0	0	GBF1
54	10:104015279	rs10748818	a	g	0.8485	0.0155	MOTORFLUX	MOTORFLUX_base	1803	0.088	0.114	1.09	[0.87, 1.37]	23.50	0.265	4.42E-01	0	0	0	0	GBF1
55	10:104015279	rs10748818	a	g	0.8523	0.0140	COGi	COGi_base	2859	-0.087	0.120	0.92	[0.72, 1.16]	25.30	0.227	4.71E-01	0	0	0	0	GBF1
56	10:104015279	rs10748818	a	g	0.8525	0.0187	SEADL	SEADL_cont	2218	0.233	0.325	0.23	[-0.40, 0.87]	4.10	0.399	4.73E-01	0	0	0	0	GBF1
57	10:104015279	rs10748818	a	g	0.8525	0.0157	INS	INS_surv	1112	-0.057	0.092	0.94	[0.79, 1.13]	11.90	0.339	5.35E-01	0	0	0	0	GBF1
58	10:104015279	rs10748818	a	g	0.8589	0.0086	CONST	CONST_base	1472	0.074	0.122	1.08	[0.85, 1.37]	0.00	0.434	5.45E-01	0	0	0	0	GBF1
59	10:104015279	rs10748818	a	g	0.8614	0.0107	HYPOSMIA	HYPOSMIA_base	1588	0.065	0.115	1.07	[0.85, 1.34]	0.00	0.894	5.71E-01	0				

1	18:40673380	rs12456492	a	g	0.6428	0.0173	DEPR	DEPR_base	2138	-0.111	0.093	0.89 [0.75, 1.07]	13.40	0.325	2.30E-01	0	0	0	0	RIT2
2	18:40673380	rs12456492	a	g	0.6338	0.0123	UPDRS2_scaled	UPDRS2_scaled_cont	2103	-0.032	0.030	-0.03 [-0.09, 0.03]	0.00	0.486	2.90E-01	0	0	0	0	RIT2
3	18:40673380	rs12456492	a	g	0.6498	0.0196	COGI	COGI_base	2859	0.086	0.091	1.09 [0.91, 1.30]	0.00	0.903	3.44E-01	0	0	0	0	RIT2
4	18:40673380	rs12456492	a	g	0.6530	0.0176	SLEEP	SLEEP_base	1724	-0.081	0.086	0.92 [0.78, 1.09]	7.90	0.368	3.48E-01	0	0	0	0	RIT2
5	18:40673380	rs12456492	a	g	0.6577	0.0185	CONST	CONST_base	1472	0.082	0.089	1.09 [0.91, 1.29]	34.00	0.195	3.57E-01	0	0	0	0	RIT2
6	18:40673380	rs12456492	a	g	0.6551	0.0202	HYPOSIMIA	HYPOSIMIA_base	1588	-0.074	0.084	0.93 [0.79, 1.09]	51.10	0.069	3.81E-01	0	0	0	0	RIT2
7	18:40673380	rs12456492	a	g	0.6343	0.0127	UPDRS1_scaled	UPDRS1_scaled_cont	2111	-0.024	0.030	-0.02 [-0.08, 0.04]	21.30	0.267	4.31E-01	0	0	0	0	RIT2
8	18:40673380	rs12456492	a	g	0.6538	0.0108	DYSKINESIAS	DYSKINESIAS_base	1232	0.078	0.108	1.08 [0.87, 1.34]	0.00	0.628	4.73E-01	0	0	0	0	RIT2
9	18:40673380	rs12456492	a	g	0.6441	0.0123	MOCA	MOCA_cont	1074	-0.090	0.127	-0.09 [-0.34, 0.16]	0.00	0.426	4.76E-01	0	0	0	0	RIT2
10	18:40673380	rs12456492	a	g	0.6452	0.0258	COGI	COGI_surv	2244	0.054	0.079	1.06 [0.90, 1.23]	0.00	0.570	4.99E-01	0	0	0	0	RIT2
11	18:40673380	rs12456492	a	g	0.6387	0.0170	UPDRS_scaled	UPDRS_scaled_cont	2994	-0.015	0.024	-0.02 [-0.06, 0.03]	0.00	0.657	5.33E-01	0	0	0	0	RIT2
12	18:40673380	rs12456492	a	g	0.6469	0.0228	HY	HY_cont	3627	-0.005	0.009	-0.00 [-0.02, 0.01]	0.00	0.662	6.13E-01	0	0	0	0	RIT2
13	18:40673380	rs12456492	a	g	0.6574	0.0172	INS	INS_base	2220	-0.036	0.073	0.96 [0.84, 1.11]	0.00	0.511	6.25E-01	0	0	0	0	RIT2
14	18:40673380	rs12456492	a	g	0.6477	0.0113	HY3	HY3_base	1289	0.059	0.121	1.06 [0.84, 1.34]	0.00	0.957	6.28E-01	0	0	0	0	RIT2
15	18:40673380	rs12456492	a	g	0.6352	0.0136	UPDRS4_scaled	UPDRS4_scaled_cont	1798	-0.011	0.026	-0.01 [-0.06, 0.04]	32.60	0.191	6.84E-01	0	0	0	0	RIT2
16	18:40673380	rs12456492	a	g	0.6355	0.0240	DEPR	DEPR_surv	1314	-0.028	0.084	0.97 [0.83, 1.15]	26.80	0.233	7.38E-01	0	0	0	0	RIT2
17	18:40673380	rs12456492	a	g	0.6387	0.0281	SEADL70	SEADL70_surv	1683	-0.017	0.094	0.98 [0.82, 1.18]	55.60	0.061	8.55E-01	0	0	0	0	RIT2
18	18:40673380	rs12456492	a	g	0.6335	0.0260	SEADL	SEADL_cont	2218	-0.042	0.243	-0.04 [-0.52, 0.43]	0.00	0.854	8.63E-01	0	0	0	0	RIT2
19	18:40673380	rs12456492	a	g	0.6402	0.0129	HY3	HY3_surv	2582	-0.011	0.066	0.99 [0.87, 1.13]	36.10	0.130	8.67E-01	0	0	0	0	RIT2
20	18:40673380	rs12456492	a	g	0.6425	0.0216	DYSKINESIAS	DYSKINESIAS_surv	1856	-0.009	0.059	0.99 [0.88, 1.11]	0.00	0.992	8.82E-01	0	0	0	0	RIT2
21	18:40673380	rs12456492	a	g	0.6326	0.0128	UPDRS3_scaled	UPDRS3_scaled_cont	2446	-0.003	0.027	-0.00 [-0.06, 0.05]	10.80	0.346	9.04E-01	0	0	0	0	RIT2
22	18:40673380	rs12456492	a	g	0.6580	0.0221	INS	INS_surv	1112	-0.005	0.070	0.99 [0.87, 1.14]	0.00	0.938	9.38E-01	0	0	0	0	RIT2
23	8:22525980	rs2280104	t	c	0.6456	0.0186	MOTORFLUX	MOTORFLUX_base	1803	-0.005	0.084	1.00 [0.84, 1.17]	0.00	0.774	9.55E-01	0	0	0	0	RIT2
24	8:22525980	rs2280104	t	c	0.3768	0.0166	MOCA	MOCA_cont	1074	-0.205	0.123	-0.20 [-0.45, 0.04]	0.00	0.448	9.58E-02	0	0	0	0	BIN3
25	8:22525980	rs2280104	t	c	0.3801	0.0057	CONST	CONST_base	1472	-0.137	0.087	0.87 [0.74, 1.03]	0.00	0.967	1.17E-01	0	0	0	0	BIN3
26	8:22525980	rs2280104	t	c	0.3745	0.0236	DYSKINESIAS	DYSKINESIAS_surv	1856	0.080	0.060	1.08 [0.96, 1.22]	0.00	0.696	1.79E-01	0	0	0	0	BIN3
27	8:22525980	rs2280104	t	c	0.3603	0.0184	SEADL	SEADL_cont	2218	-0.320	0.240	-0.32 [-0.79, 0.15]	15.70	0.307	1.83E-01	0	0	0	0	BIN3
28	8:22525980	rs2280104	t	c	0.3772	0.0235	COGI	COGI_base	2859	0.118	0.089	1.13 [0.95, 1.34]	0.00	0.813	1.83E-01	0	0	0	0	BIN3
29	8:22525980	rs2280104	t	c	0.3745	0.0062	DYSKINESIAS	DYSKINESIAS_base	1232	0.122	0.102	1.13 [0.92, 1.38]	0.00	0.713	2.33E-01	0	0	0	0	BIN3
30	8:22525980	rs2280104	t	c	0.3752	0.0181	COGI	COGI_surv	2244	0.086	0.073	1.09 [0.94, 1.26]	22.00	0.248	2.42E-01	0	0	0	0	BIN3
31	8:22525980	rs2280104	t	c	0.3638	0.0229	SEADL70	SEADL70_surv	1683	0.109	0.095	1.12 [0.93, 1.34]	40.10	0.154	2.52E-01	0	0	0	0	BIN3
32	8:22525980	rs2280104	t	c	0.3771	0.0254	UPDRS2_scaled	UPDRS2_scaled_cont	2103	0.023	0.029	0.02 [-0.03, 0.08]	0.00	0.709	4.42E-01	0	0	0	0	BIN3
33	8:22525980	rs2280104	t	c	0.3679	0.0155	MOTORFLUX	MOTORFLUX_base	1803	-0.064	0.083	0.94 [0.80, 1.10]	0.00	0.429	4.44E-01	0	0	0	0	BIN3
34	8:22525980	rs2280104	t	c	0.3752	0.0275	UPDRS4_scaled	UPDRS4_scaled_cont	1798	-0.017	0.025	-0.02 [-0.07, 0.03]	0.00	0.705	5.12E-01	0	0	0	0	BIN3
35	8:22525980	rs2280104	t	c	0.3696	0.0184	DEPR	DEPR_surv	1314	0.044	0.080	1.05 [0.89, 1.22]	12.70	0.334	5.80E-01	0	0	0	0	BIN3
36	8:22525980	rs2280104	t	c	0.3858	0.0325	UPDRS3_scaled	UPDRS3_scaled_cont	2446	-0.013	0.026	-0.01 [-0.06, 0.04]	0.00	0.880	6.20E-01	0	0	0	0	BIN3
37	8:22525980	rs2280104	t	c	0.3816	0.0206	HYPOSIMIA	HYPOSIMIA_base	1588	-0.039	0.082	0.96 [0.82, 1.13]	53.50	0.056	6.38E-01	0	0	0	0	BIN3
38	8:22525980	rs2280104	t	c	0.3807	0.0299	UPDRS_scaled	UPDRS_scaled_cont	2994	-0.010	0.024	-0.01 [-0.06, 0.04]	0.00	0.482	6.96E-01	0	0	0	0	BIN3
39	8:22525980	rs2280104	t	c	0.3829	0.0210	SLEEP	SLEEP_base	1724	0.024	0.085	1.02 [0.87, 1.21]	37.10	0.145	7.81E-01	0	0	0	0	BIN3
40	8:22525980	rs2280104	t	c	0.3779	0.0070	HY3	HY3_base	1289	0.027	0.116	1.03 [0.82, 1.29]	0.00	0.798	8.17E-01	0	0	0	0	BIN3
41	8:22525980	rs2280104	t	c	0.3727	0.0250	DEPR	DEPR_base	2138	0.017	0.091	1.02 [0.85, 1.22]	0.00	0.875	8.52E-01	0	0	0	0	BIN3
42	8:22525980	rs2280104	t	c	0.3781	0.0184	INS	INS_base	2220	-0.012	0.071	0.99 [0.86, 1.14]	0.00	0.969	8.62E-01	0	0	0	0	BIN3
43	8:22525980	rs2280104	t	c	0.3841	0.0071	INS	INS_surv	1112	-0.007	0.067	0.99 [0.87, 1.13]	0.00	0.806	9.12E-01	0	0	0	0	BIN3
44	8:22525980	rs2280104	t	c	0.3896	0.0274	HY	HY_cont	3627	0.000	0.009	-0.00 [-0.02, 0.02]	25.90	0.190	9.84E-01	0	0	0	0	BIN3
45	8:22525980	rs2280104	t	c	0.3728	0.0198	MOTORFLUX	MOTORFLUX_surv	1709	-0.001	0.050	1.00 [0.91, 1.10]	0.00	0.777	9.85E-01	0	0	0	0	BIN3
46	8:22525980	rs2280104	t	c	0.3737	0.0265	UPDRS1_scaled	UPDRS1_scaled_cont	2111	0.000	0.029	-0.00 [-0.06, 0.06]	0.00	0.806	9.93E-01	0	0	0	0	BIN3
47	8:22525980	rs2280104	t	c	0.3712	0.0211	MMSE	MMSE_cont	2114	0.000	0.046	-0.00 [-0.09, 0.09]	0.00	0.475	9.95E-01	0	0	0	0	BIN3
48	11:133787001	rs3802920	t	g	0.2152	0.0183	UPDRS4_scaled	UPDRS4_scaled_cont	1798	0.048	0.030	0.05 [-0.01, 0.11]	47.20	0.092	1.06E-01	0	0	0	0	IGSF9B
49	11:133787001	rs3802920	t	g	0.2189	0.0163	COGI	COGI_base	2859	0.155	0.101	1.17 [0.96, 1.42]	0.00	0.586	1.26E-01	0	0	0	0	IGSF9B
50	11:133787001	rs3802920	t	g	0.2157	0.0143	DYSKINESIAS	DYSKINESIAS_surv	1856	0.087	0.067	1.09 [0.96, 1.24]	0.00	0.802	1.91E-01	0	0	0	0	IGSF9B
51	11:133787001	rs3802920	t	g	0.2153	0.0119	MOTORFLUX	MOTORFLUX_surv	1709	-0.059	0.058	0.94 [0.84, 1.06]	0.00	0.568	3.10E-01	0	0	0	0	IGSF9B
52	11:133787001	rs3802920	t	g	0.2053	0.0157	SEADL	SEADL_cont	2218	-0.283	0.281	-0.28 [-0.83, 0.27]	0.00	0.729	3.15E-01	0	0	0	0	IGSF9B
53	11:133787001	rs3802920	t	g	0.2199	0.0205	HYPOSIMIA	HYPOSIMIA_base	1588	-0.094	0.094	0.91 [0.76, 1.09]	0.00	0.861	3.17E-01	0	0	0	0	IGSF9B
54	11:133787001	rs3802920	t	g	0.2213	0.0194	INS	INS_base	2220	0.077	0.084	1.08 [0.92, 1.27]	28.20	0.203	3.60E-01	0	0	0	0	IGSF9B
55	11:133787001	rs3802920	t	g	0.2136	0.0145	MMSE	MMSE_cont	2114	0.047	0.053	0.05 [-0.06, 0.15]	0.00	0.863	3.80E-01	0	0	0	0	IGSF9B
56	11:133787001	rs3802920	t	g	0.2127	0.0128	INS	INS_surv	1112	-0.061	0.076	0.94 [0.81, 1.09]	0.00	0.777	4.19E-01	0	0	0	0	IGSF9B
57	11:133787001	rs3802920	t	g	0.2106	0.0165	UPDRS_scaled	UPDRS_scaled_cont	2994	0.019	0.028	0.02 [-0.04, 0.07]	17.50	0.282	4.96E-01	0	0	0	0	IGSF9B
58	11:133787001	rs3802920	t	g	0.2268	0.0009	DYSKINESIAS	DYSKINESIAS_base	1232	0.075	0.120	1.08 [0.85, 1.36]	0.00	0.758	5.31E-01	0	0	0	0	IGSF9B
59	11:133787001	rs3802920	t	g	0.2108	0.0197	UPDRS3_scaled	UPDRS3_scaled_cont	2446	0.018	0.031	0.02 [-0.04, 0.08]	0.00	0.786	5.54E-01	0	0	0	0	IGSF9B
60	11:133787001	rs3802920	t	g	0.2210	0.0155	DEPR	DEPR_surv	1314	0.052	0.093	1.05 [0.88, 1.26]	47.60	0.090	5.81E-01	0	0	0	0	IGSF9B
61	11:133787001	rs3802920	t	g	0.2089	0.0122	MOCA</													

base, logistic regression model at the baseline; surv, Cox survival model; cont, linear mixed effect model

Supplemental Table 5 The Estimated Study Size to Detect at Least One Variant with Genome-wide Significance

Phenotype	Top_SNP	A1	A2	MAF	BETA	SE	P	N	N_Multiplier	N_required	Sig_in_1.3_larger_N
base_HYPOSMIA	1:56034603	C	A	0.119	0.570	0.118	1.49E-06	1588	1.30	2064	TRUE
base_MOTORFLUX	2:170778662	C	G	0.143	0.734	0.162	6.08E-06	1568	1.48	2325	FALSE
base_SLEEP	17:27353069	A	G	0.188	0.592	0.118	5.56E-07	1724	1.20	2062	TRUE
base_HY3	2:232324780	A	G	0.349	0.610	0.122	5.71E-07	1289	1.20	1545	TRUE
base_CONST	2:18336194	A	G	0.269	0.479	0.097	8.59E-07	1472	1.24	1825	TRUE
base_INS	10:112956055	A	G	0.318	-0.455	0.083	4.74E-08	2220	1.00	2212	TRUE
base_DYSKINESIAS	1:182045339	C	G	0.066	0.898	0.212	2.25E-05	1232	1.70	2100	FALSE
base_DEPR	17:33680811	A	C	0.164	0.554	0.114	1.22E-06	2138	1.28	2730	TRUE
base_COGi	8:116961224	A	G	0.080	1.013	0.190	9.77E-08	1538	1.05	1612	TRUE
cont_HY	10:27370747	G	A	0.063	0.098	0.020	8.68E-07	3627	1.24	4501	TRUE
cont_SEADL	11:88031232	C	T	0.299	1.469	0.281	1.74E-07	2218	1.09	2424	TRUE
cont_UPDRS	6:25370200	T	G	0.050	0.486	0.101	1.41E-06	1792	1.29	2318	TRUE
cont_UPDRS4_scaled	10:90420315	T	G	0.240	0.201	0.041	1.14E-06	1798	1.27	2283	TRUE
cont_UPDRS2_scaled	19:17340155	A	G	0.074	0.294	0.060	9.66E-07	2301	1.25	2881	TRUE
cont_MMSE	6:2977327	A	G	0.056	-0.709	0.135	1.51E-07	1066	1.08	1153	TRUE
cont_UPDRS3_scaled	5:60307904	G	A	0.409	0.149	0.031	1.09E-06	2822	1.27	3570	TRUE
cont_UPDRS_scaled	12:129483261	T	C	0.139	-0.298	0.058	2.96E-07	1108	1.14	1261	TRUE
cont_MOCA	14:54619316	C	T	0.188	-0.937	0.199	2.61E-06	1074	1.37	1468	FALSE
surv_SEADL70	22:50944128	A	G	0.288	0.488	0.103	2.03E-06	1683	1.34	2249	FALSE
surv_MOTORFLUX	8:142310903	T	G	0.134	0.431	0.087	6.21E-07	1709	1.21	2062	TRUE
surv_HY3	9:108058562	A	T	0.075	0.711	0.129	3.46E-08	1890	0.98	1844	TRUE
surv_INS	2:241442030	T	C	0.060	0.703	0.144	9.75E-07	1112	1.25	1393	TRUE
surv_DYSKINESIAS	12:121627464	A	T	0.068	0.509	0.100	3.76E-07	1856	1.16	2151	TRUE
surv_DEPR	14:52568619	C	T	0.095	0.640	0.127	4.66E-07	1395	1.18	1645	TRUE
surv_COGi	21:17309623	G	C	0.083	0.912	0.170	7.76E-08	1132	1.03	1167	TRUE

Top_SNP, the SNP with the smallest p-value;

Multiplier, Multiplier of the N to have enough power to detect the Top_SNP at the significance level of 5E-8;

N_required, The total number required to detect the Top_SNP at the significance level of 5E-8;

Sig_in_1.3_larger_N, Whether or not obtaining at least one genome-wide significant variant for that phenotype if the N was 1.3 times larger;

base, logistic regression model at the baseline; surv, Cox survival model; cont, linear mixed effect model

CONST, constipation; COGi, cognitive impairment; INS, insomnia; SLEEP, daytime sleepiness; MOTORFLUX, motor fluctuations; HY3, Hoehn Yahr scale 3 or greater; RBD, REM sleep behavior

disorder; DEPR, depression; MMSE, Mini Mental State Examination; Montreal Cognitive Assessment, SEADL, Schwab and England Activities of Daily Living Scale; UPDRS, Unified Parkinson

Disease Rating Scale; MDS-UPDRS, Movement Disorder Society revised version of UPDRS."

Appendix A: The description of study cohorts

Deprenyl and Tocopherol Antioxidative Therapy of Parkinsonism (DATATOP) was a randomized clinical trial conducted between September 1987 and November 1989 at 28 sites across US and Canada. The primary objective was to test the efficacy of deprenyl and/or tocopherol. 800 patients with Parkinson’s disease diagnosed within 5 years and not requiring symptomatic treatment were observed for up to 2 years.¹ The study was supported by a Public Health Service grant (NS24778) from the National Institute of Neurological Disorders and Stroke; by grants from the General Clinical Research Centers Program of the National Institutes of Health at Columbia University (RR00645), the University of Virginia (RR00847), the University of Pennsylvania (RR00040), the University of Iowa (RR00059), Ohio State University (RR00034), Massachusetts General Hospital (RR01066), the University of Rochester (RR00044), Brown University (RR02038), Oregon Health Sciences University (RR00334), Baylor College of Medicine (RR00350), the University of California, San Diego (RR00827), Johns Hopkins University (RR00035), the University of Michigan (RR00042), and Washington University (RR00036); the Parkinson's Disease Foundation at Columbia-Presbyterian Medical Center, New York; the National Parkinson Foundation, Miami; the Parkinson Foundation of Canada, Toronto; the United Parkinson Foundation, Chicago; the American Parkinson's Disease Association, New York; and the University of Rochester, Rochester, N.Y.

Drug Interaction with Genes in Parkinson's Disease (DIGPD) is a cohort with 413 patients with Parkinson’s disease diagnosed by UK Parkinson’s disease society brain bank clinical diagnostic (UKPDSBB) criteria with disease duration less than 5 years at the entry.² It is an ongoing study since 2009, and the participants are followed for up to 7 years at eight sites in France. (Corvol et al., in press in Neurology). DNA samples were collected from all of them. DIGPD is sponsored by Assistance Publique Hôpitaux de Paris, funded by a grant from the French Ministry of Health (PHRC 2008, AOM08010) and a grant from the Agence Nationale pour la Sécurité des Médicaments (ANSM 2013).

Harvard Biomarkers Study (HBS) is a longitudinal case-control study. More than 2,700 individuals with early-stage PD, patients with memory impairment, and controls without

neurological disease were enrolled and longitudinally phenotyped since 2008.³ HBS was supported by the Harvard NeuroDiscovery Center, MJFF, NINDS U01NS082157, U01NS100603, and the Massachusetts Alzheimer's Disease Research Center NIA P50AG005134.

NIH Exploratory Trials in Parkinson's Disease Large Simple Study 1 (NET-PD LS1) was a randomized study conducted between March 2007 and September 2013 to determine if the nutritional supplement creatine slows the clinical progression of Parkinson's disease over time. 1741 patients from 50 sites in the US and Canada participated.⁴ They were within 5 years from diagnosis. The plan was for them to be followed for at least 5 years, but the study ended early for futility based on an interim analysis at which point the median follow-up time was 4 years. Financial support for the LS-1 study was provided by National Institute of Neurological Disorders and Stroke (NINDS) grant U01NS43128.

Oslo PD study[Citation error] (Oslo) is an ongoing study since 2007, with 317 patients diagnosed with ULPDSBB criteria with modification of allowing family history. The participants are being followed up to 6 years in prospective (30 years in retrospective) at Oslo University Hospital in Norway.⁵ Oslo PD is supported by the Research Council of Norway and South-Eastern Norway Regional Health Authority.

ParkFit cohort was originally a randomized trial evaluating a multifaceted behavioural change programme to increase physical activities in patients with Parkinson's disease.⁶ The study conducted from September 2008 to February 2012 at a single center in the Netherlands, with 586 patients with Parkinson's disease diagnosed by UKPDSBB, with Hoehn Yahr stage 3 or lower, and with sedentary lifestyle at the entry. They were followed up for 2 years. The primary objective was concluded as not significant⁶. ParkFit is supported by ZonMw (the Netherlands Organization for Health Research and Development (75020012)) and the Michael J Fox Foundation for Parkinson's research, VGZ (health insurance company), GlaxoSmithKline, and the National Parkinson Foundation.

The Norwegian ParkWest study (ParkWest) is an ongoing prospective longitudinal multicenter cohort study of patients with incident Parkinson's disease from Western and Southern Norway, designed to study the incidence, neurobiology and prognosis of PD.⁷ Between November 1st 2004 and 31st of August 2006, all new cases of Parkinson Disease within the study area (Sogn and Fjordane, Hordaland, Rogaland and Aust-Agder) were recruited, and since the start of the

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study 212 of these patients and their age-/sex-matched control group were followed. The Norwegian ParkWest study is supported by the Research Council of Norway, the Western Norway Regional Health Authority, Stavanger University Hospital Research Funds, and the Norwegian Parkinson's Disease Association.

The National Institute of Neurological Disorders and Stroke (NINDS) Parkinson's Disease Biomarker Program (PDBP) is aiming to discover new diagnostic and progression biomarkers for Parkinson's disease.⁸ It is a combined cohort of 9 PDBP-funded research studies. The members have various stages of Parkinson's disease and recruited throughout the United States. Parkinsonism: Incidence and Cognitive and Non-motor heterogeneity In Cambridgeshire (PICNICS) is a population-based longitudinal study of 282 incident PD cases recruited between 2008 and 2013 with ongoing follow-up at 18 month intervals.^{9,10} PD cases were diagnosed based on the UKPDSBB criteria, and followed up at a single center in the UK. PICNICS has received funding from the Cure Parkinson's Trust, the Van Geest Foundation and is supported by the the National Institute of Health Research Cambridge Biomedical Research Centre.

Parkinson's progression markers initiative (PPMI) is an ongoing study started on July 2010, enrolling 424 patients with Parkinson's disease diagnosed within 2 years from the study entry date.¹¹ The study sites are located in 33 sites across the US, Europe, Israel and Australia¹¹. PPMI is supported by the Michael J Fox Foundation for Parkinson's Research.

Parkinson Research Examination of CEP1348 Trial (PreCEPT) is a clinical trial of the mixed lineage kinase inhibitor CEP-1357,4 sponsored by Cephalon, Inc. (West Chester, PA) and H. Lundbeck A/S (Valby-Copenhagen, Denmark). The study was conducted at 65 sites in North America. The trial enrolled 806 early, untreated PD patients within one year from the onset. The original trial was started in April 2002 and terminated in August 2005 due to the futility, but the participants were continuously followed-up in the prospective observational study (PostCEPT).¹² The studies were funded by NINDS 5U01NS050095-05, Department of Defense Neurotoxin Exposure Treatment Parkinson's Research Program. Grant Number: W23RRYX7022N606, the Michael J Fox Foundation for Parkinson's research, Parkinson's Disease Foundation, Lundbeck Pharmaceuticals. Cephalon Inc, Lundbeck Inc, John Blume Foundation, Smart Family Foundation, RJG Foundation, Kinetics Foundation, National Parkinson Foundation, Amarin Neuroscience LTD, CHDI Foundation Inc, National Institutes of Health (NHGRI, NINDS), Columbia Parkinson's Disease Research Center.

Profiling Parkinson's disease study (ProPark) is an ongoing study started from May 2003. Initially, 420 patients recruited in several sites in the Netherlands by March 2006.¹³ Patients were diagnosed with UKPDSBB criteria and in various disease durations at the enrollment. They are evaluated annually with the SCOPA scale. This study is funded by the Alkemade-Keuls Foundation, Stichting Parkinson Fonds, Parkinson Vereniging, The Netherlands Organisation for Health Research and Development.

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References

1 Parkinson Study Group. DATATOP: a multicenter controlled clinical trial in early
2 Parkinson’s disease. Parkinson Study Group. *Arch Neurol* 1989; **46**: 1052–60.
3 Corvol J-C, Artaud F, Cormier-Dequaire F, *et al.* Longitudinal analysis of impulse control
4 disorders in Parkinson disease. *Neurology* 2018; **91**: e189–201.
5 Locascio JJ, Eberly S, Liao Z, *et al.* Association between α -synuclein blood transcripts and

- early, neuroimaging-supported Parkinson's disease. *Brain* 2015; **138**: 2659–71.
- 4 Writing Group for the NINDS Exploratory Trials in Parkinson Disease Investigators. Effect of creatine monohydrate on clinical progression in patients with Parkinson disease: a randomized clinical trial. *JAMA* 2015; **313**: 584–93.
- 5 Pihlstrøm L, Morset KR, Grimstad E, Vitelli V, Toft M. A cumulative genetic risk score predicts progression in Parkinson's disease. *Mov Disord* 2016; **31**: 487–90.
- 6 van Nimwegen M, Speelman AD, Overeem S, *et al.* Promotion of physical activity and fitness in sedentary patients with Parkinson's disease: randomised controlled trial. *BMJ* 2013; **346**: f576.
- 7 Alves G, Müller B, Herlofson K, *et al.* Incidence of Parkinson's disease in Norway: the Norwegian ParkWest study. *J Neurol Neurosurg Psychiatry* 2009; **80**: 851–7.
- 8 Rosenthal LS, Drake D, Alcalay RN, *et al.* The NINDS Parkinson's disease biomarkers program. *Mov Disord* 2016; **31**: 915–23.
- 9 Breen DP, Vuono R, Nawarathna U, *et al.* Sleep and circadian rhythm regulation in early Parkinson disease. *JAMA Neurol* 2014; **71**: 589–95.
- 10 Evans JR, Cummins G, Breen DP, *et al.* Comparative epidemiology of incident Parkinson's disease in Cambridgeshire, UK: Table 1. *J Neurol Neurosurg Psychiatry* 2016; **87**: 1034–6.
- 11 Marek K, Jennings D, Lasch S, *et al.* The Parkinson Progression Marker Initiative (PPMI). *Prog Neurobiol* 2011; **95**: 629–35.
- 12 Ravina B, Tanner C, Dieuliis D, *et al.* A longitudinal program for biomarker development in Parkinson's disease: a feasibility study. *Mov Disord* 2009; **24**: 2081–90.
- 13 Verbaan D, Marinus J, Visser M, van Rooden SM, Stiggelbout AM, van Hilten JJ. Patient-reported autonomic symptoms in Parkinson disease. *Neurology* 2007; **69**: 333–41.

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